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14. ABSTRACT
Alcohol use disorders (AUDs) and PTSD commonly co-occur, complicate assessment and treatment, and worsen clinical outcomes in veterans with both conditions. AUDs are potential consequences of PTSD, as many veterans may use alcohol in an attempt to "self-medicate" or ameliorate PTSD symptoms such as hyperarousal or emotional numbing. AUDs may also be a risk factor for the development of PTSD and may exacerbate PTSD symptom severity and impairment. Treatment for co-occurring PTSD and alcohol dependence among veterans is challenging. To date there has been little research to develop pharmacotherapies that would, ideally, reduce both alcohol use and PTSD symptom severity in patients with both of these conditions. Topiramate is one of the few medications for alcohol dependence that has also been separately tested as a potential medication to treat PTSD. Topiramate's efficacy in alcohol dependence in patients without PTSD has been shown in two recent large controlled trials. Open trials have suggested that topiramate may be effective in reducing PTSD symptoms in patients without AUDs, and a number of small controlled trials have also produced promising results. The PI recently completed the first pilot clinical trial of topiramate treatment in veterans with both alcohol dependence and PTSD, and preliminary analyses demonstrate feasibility, safety, tolerability, and efficacy in reducing alcohol use. Results also provide support for testing topiramate's potential efficacy in reducing PTSD symptoms.

15. SUBJECT TERMS
Pharmacotherapy, Co-occurring Disorders, PTSD, alcohol dependence, topiramate

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INTRODUCTION:

The overall objective of the project is to improve the care of veterans with alcohol dependence and co-occurring PTSD. The investigators are conducting a controlled clinical trial to test the efficacy of topiramate treatment in reducing alcohol use in patients with PTSD.

Alcohol use disorders (AUDs) and PTSD commonly co-occur, complicate assessment and treatment, and worsen clinical outcomes in veterans with both conditions. AUDs are potential consequences of PTSD, as many veterans may use alcohol in an attempt to "self-medicate" or ameliorate PTSD symptoms such as hyperarousal or emotional numbing. AUDs may also be a risk factor for the development of PTSD and may exacerbate PTSD symptom severity and impairment. Treatment for co-occurring PTSD and alcohol dependence among veterans is challenging. To date there has been little research to develop pharmacotherapies that would, ideally, reduce both alcohol use and PTSD symptom severity in patients with both of these conditions. Topiramate is one of the few medications for alcohol dependence that has also been separately tested as a potential medication to treat PTSD. Topiramate's efficacy in alcohol dependence in patients without PTSD has been shown in two recent large controlled trials. Open label trials have suggested that topiramate may be effective in reducing PTSD symptoms in patients without AUDs, and a number of small controlled trials have also produced promising results. The PI recently completed the first pilot clinical trial of topiramate treatment in veterans with both alcohol dependence and PTSD, and preliminary analyses demonstrate feasibility, safety, tolerability, and possible efficacy in reducing alcohol use as well as PTSD symptoms.

This project consists of a controlled clinical trial of topiramate treatment to reduce alcohol use and PTSD symptoms in veterans with these co-occurring disorders. The specific aims are to: 1) definitively test the efficacy of topiramate in reducing alcohol use in veterans with PTSD and alcohol dependence; 2) test the efficacy of topiramate to reduce PTSD symptoms; and 3) explore if measures of impulsivity and decision-making predict treatment response and improve with topiramate therapy. To achieve these aims, we are conducting a prospective randomized double-blind controlled parallel-groups clinical trial of topiramate or placebo up to 300 mg per day, combined with weekly alcohol counseling, over a 12-week treatment period with a week 16 follow-up. The study population will consist of 150 male and female veterans between the ages of 18-69 who have concurrent diagnoses of alcohol dependence and PTSD. Subjects will meet with research staff weekly to receive study medication, manualized alcohol counseling, and research assessments. The primary treatment outcome will be the percent of days of heavy drinking; the secondary outcome will be PTSD symptom severity. Exploratory measures will include assessments of impulsivity and decision-making.

A.1. PRIMARY AIM: To determine if topiramate treatment reduces alcohol use in veterans with PTSD

1.a. The primary aim is to definitively test the efficacy of topiramate in reducing alcohol use in veterans with PTSD and alcohol dependence.
1.b. The primary outcome will be the percent of heavy drinking days over the course of the study as measured by the Timeline Followback.

1.c. The primary hypothesis is that topiramate treatment will be more efficacious than placebo in reducing the proportion of heavy drinking days.

This hypothesis will be tested through a mixed-model statistical analysis of the between-groups differences in the proportion of heavy drinking days over the course of the clinical trial.

A.2. SECONDARY AIMS: To determine if topiramate reduces PTSD symptoms and alcohol use (using other alcohol use measures) in these patients.

The *secondary aims* are*:*

2.1.a To determine whether topiramate will be associated with a significant reduction in PTSD symptoms from baseline to the end of the trial, as measured by the PTSD Checklist (PCL); and to determine whether topiramate will be more efficacious than placebo.

2.2.a To determine whether topiramate treatment will be associated with significant reductions in other alcohol use measures (drinking days/week, drinks per drinking day, alcohol craving, and urine Ethyl Glucuronide [EtG]) from baseline to end of treatment; and to determine whether topiramate will be more efficacious than placebo

The *secondary hypotheses* are:

2.1.b Topiramate treatment -- combined with Medical Management alcohol counseling and added to ongoing TBI treatment as usual --will be associated with a significant reduction in PTSD symptoms from baseline to the end of the trial, as measured by the PTSD Checklist (PCL) from baseline to end of treatment; and there will be a significant effect of the treatment group, with the topiramate treatment group showing a greater reduction in PCL scores compared to placebo controls.

2.2.b Topiramate treatment -- combined with Medical Management alcohol counseling and added to ongoing PTSD treatment as usual --will be associated with a significant reduction in scores of other alcohol use measures from baseline to end of treatment; and there will be a significant effect of the treatment group, with the topiramate treatment group showing a greater reduction in scores on various alcohol use measures compared to placebo controls.

These hypotheses will be tested:

2.1.c Through a mixed-model statistical analysis of the within-topiramate group and between-groups differences in PCL scores over the course of the clinical trial.

2.2.c Through a mixed-model statistical analysis of the within-topiramate group and between-groups analysis differences in scores on alcohol use measures (drinking days/week, drinks per drinking day, alcohol craving and urine Ethyl Glucuronide [EtG]) over the course of the clinical trial.

A.3. EXPLORATORY AIMS:

The exploratory aims are:

3.1 Measure impulsivity, decision-making, and risk-taking at baseline to assess the relationship between these domains and:

- alcohol use at baseline
- alcohol use over the course of the study

3.2 Assess the relationship between *changes* in alcohol use over the course of the study and *changes* in:

- impulsivity
- risk-taking
- decision-making

3.3 Assess the effects of topiramate versus placebo treatment on:

- impulsivity
- risk-taking
- verbal fluency, verbal memory

The exploratory hypotheses are:

3.1 High impulsivity, high risk-taking, and poor decision-making at baseline will be associated with higher levels of alcohol use at baseline and over the course of the study;

3.2 Reductions in alcohol use will be associated with reductions in impulsivity and risk taking, and improvement in decision-making;

3.3 Topiramate will be associated with greater reductions in impulsivity and risk-taking, but also with greater impairment of verbal fluency and memory than placebo.

These hypotheses will be tested with mixed models similarly to the primary and secondary hypotheses.

3.1 is assessed by the effect of baseline impulsivity and risk-taking (tested separately) on alcohol use over time.

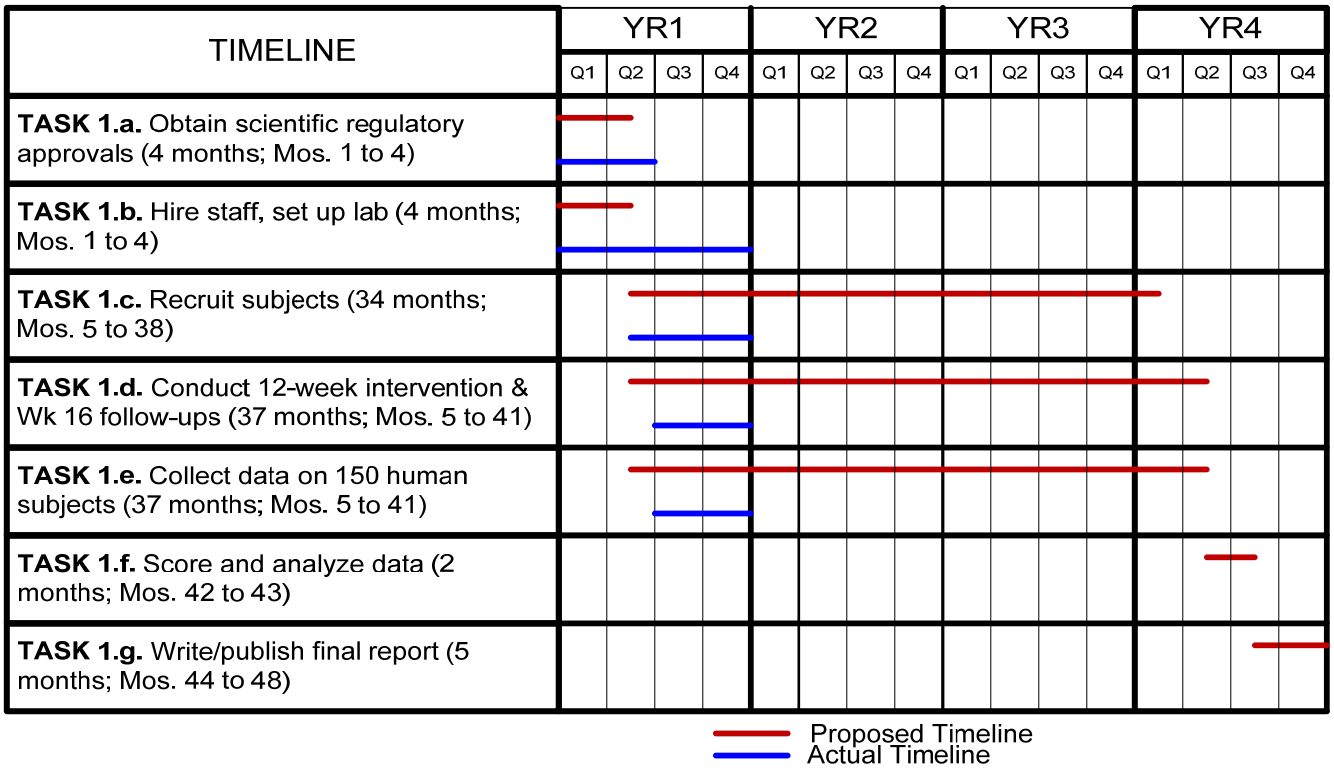
3.2 is tested by estimating subject-specific slopes from random coefficients mixed models predicting changes in alcohol use, impulsivity, and risk-taking, and calculating the Pearson correlation coefficients between slopes of change in alcohol use and changes in impulsivity and risk-taking.

3.3 is tested by the Group by Time interaction term in the mixed models predicting impulsivity, risk-taking, verbal fluency and verbal memory, from treatment group and time, with baseline values as covariates.

BODY:

This study was initiated 29 September 2012. Year 1 of this project covers the time period September 30, 2012 through September 29, 2013. As of September 29, 2013 we have met our overall Year 1 goals in terms of gaining all regulatory approvals, hiring staff, and setting up the lab. Additionally, we have been recruiting subjects and administering study intervention since the 2nd quarter of Year 1. Two final tasks need to be accomplished in order to complete lab set-up: roll-out the remaining 20 forms in the Access database/interface and employ a 3rd Study Coordinator to bolster recruitment efforts. All tasks for Year 1 were predetermined in the approved Statement of Work; the steps taken to accomplish these tasks are outlined in further detail below.

STATEMENT OF WORK - TIMELINE



Task 1

Test the hypothesis that veterans with alcohol dependence and PTSD assigned to topiramate (TOP) treatment will have fewer heavy alcohol drinking days over the 12 weeks of the treatment trial than subjects receiving placebo (PBO)

Timeline: *Months 1-4:* production and all approvals of human use protocols, hiring staff, start-up/set up lab; *months 5-38:* recruitment of subjects; *months 5-41*: conduct treatment intervention, follow-ups; *months 5-41*: complete data collection on 150 subjects; *months 42-43*: analyze data; *months 44-48*: final report/manuscripts written and submitted.

TASK 1.a. ***Months 1-4:*** **production and all approvals of human use protocols, hiring staff, start-up/set up lab**

All DOD-funded studies that take place at the San Francisco VA Medical Center are required to receive approval from the local IRB [University of California, San Francisco Committee on Human Research (UCSF CHR)], the VA Clinical Research Workgroup (VA CRW), the Information Security Officer (ISO), the Privacy Officer (PO), the UCSF Clinical and Translational Science Institute (CTSI), the Subcommittee on Research Safety (SRS), and the VA Research and Development Committee (VA R&DC). In addition to gaining approval from the various regulatory bodies, we also applied for a NIH/NIAAA Certificate of Confidentiality (NIH/NIDA CoC), an IND exemption from the Federal Drug Association (FDA) and a Biological Use Authorization (BUA) for Clinical Research from the VA Biosafety Subcommittee as extra protection for our research subjects and study staff. All required approvals were received by 2/26/13 (Month 5).

The hiring of lab personnel is near complete. As of 9/29/13, we have hired the following essential employees: 1 Lab Manager, 2 Study Coordinators, 1 Research Psychologist, 1 Research Statistician, 1 Research Physician, 1 Research Nurse Practitioner, and 1 Database Developer/Manager. Additional staff that either work at a less percent effort or volunteer include: 2 Study Physicians, 1 Research Psychologist, 2 Nurse Practitioners, and 1 Data Programmer. We are also supporting a percent effort of our co-investigators. The last addition to our research lab includes a 3rd Study Coordinator to support our steady but slow recruitment efforts.

To set-up the lab, we purchased various materials and supplies, computers, and other subject- and research-related items, such as computer software, database software/tools, and established various vendor accounts. As of 9/29/13, we have purchased all materials necessary to conduct the clinical trial. Study staff has been trained on the administration of all measures and procedures. The last outstanding component of our lab set-up is the database. Of the 57 measures and procedures that we plan to collect on-line, 37 are in active use. The final step for lab set-up will be to roll-out the remaining 20 forms.

TASK 1.b. ***Months 5-38:*** **recruitment of subjects**

Subject recruitment began on 2/27/13 and the first informed consent was signed on 3/20/13. One hundred and seventy seven potential subjects were referred to the study, either by self-referral or by medical/mental health practitioners. Seventy two prospective subjects were pre-screened for the study; 14 were enrolled (signed informed consent form) and 9 randomly assigned to treatment with topiramate (top) or placebo (PLA). The cohort is all male (n=9, 100%) and predominantly Caucasian (n=6, 67%). The planned rate of recruitment was 1 subject per week or 4 subjects per month; however, in order to complete

recruitment according to schedule, we will need to randomize 5 subjects per month for the next 26 months. We are in the process of hiring a 3rd study coordinator who will focus on recruitment efforts.

TASK 1.c. ***Months 5-41*: conduct treatment intervention, follow-ups**

Inclusion for this study is based on the outcome of a screening phase which includes medical assessment, structured psychological interviews to determine diagnostic eligibility [Structured Clinical Interview for DSM-IV (SCID) and the Clinician Administered PTSD Scale (CAPS)] and additional measures to assess psychiatric severity and medical utilization. Of the 9 subjects randomized, one was withdrawn from the study due to a combination of symptoms: mild confusion, increased anxiety, and appetite/weight loss. One subject dropped out at Week 2 due to side effects, presumably related to the study medication. Subjects that attend the Week 12 study visit are considered "completers". As of 9/29/13, only 6 of the 9 enrolled could have attended Week 12, of which 4 (67%) are considered "completers". Of all subjects enrolled, the average number of study visits attended is 9 (81%).

TASK 1.d. ***Months 5-41*: complete data collection on 150 subjects**

In progress - not complete at this time.

TASK 1.e. ***Months 42-43*: analyze data**

Not complete at this time.

TASK 1.f. ***Months 44-48*: final report/manuscripts written and submitted.**

Not complete at this time.

Task 2.

Test the hypothesis that veterans with alcohol dependence and PTSD assigned to topiramate (TOP) treatment will have lower PTSD symptom severity over the 12 weeks of the treatment trial than subjects receiving placebo (PBO)

Timeline*: *same as Task 1

In progress - not complete at this time.

Task 3.
Explore the role of impulsivity and decision-making in the treatment of alcohol dependence and PTSD.

Subtask 3.a. To assess the predictive value of baseline measures of decision-making and impulsivity as related to study retention and alcohol use outcomes.
Subtask 3.b. To test whether reduction in alcohol use is accompanied by reductions in impulsivity/risk-taking and improvement in decision-making in veterans with alcohol dependence and PTSD.
Subtask 3.c. To test whether topiramate is more efficacious than placebo in reducing impulsivity/risk-taking and improving decision-making.

***Design*:** same as Task 1
***Human subjects*:** same as Task 1
Methods: Subjects will meet with research staff weekly to receive study medication, manualized alcohol counseling, and research assessments.
Assessments: The exploratory outcomes will be impulsivity/risk-taking as measured by the Balloon Analogue Risk Task (BART) and decision-making as measured by the Delay Discounting Test (DD).

***Outcomes, products and deliverables*:** The *exploratory hypotheses* are:

Subtask 3a: high baseline impulsivity/risk-taking and poor decision-making will be associated with poor retention and worse alcohol use outcome over the course of the trial
Subtask 3b: reductions in alcohol use over the course of the trial will be associated with reduced impulsivity/risk-taking and improved decision-making over the course of the trail
Subtask 3c: topiramate treatment will be more efficacious than placebo in reducing impulsivity and risk-taking and improving decision-making.
These hypothesis will be tested through mixed-model statistical analyses of the between-groups differences in the appropriate measures.

Timeline*:** ***same as Task 1

In progress - not complete at this time.

KEY RESEARCH ACCOMPLISHMENTS: Bulleted list of key research accomplishments emanating from this research.

1. Created a modified version of the NIAAA Medical Management Treatment Manual, 2010 edition. This adaptation takes into consideration the study population, the nature of the medication, the context of a clinical trial, and the varying levels of medical training among study clinicians. 4/23/13
2. Developed a glaucoma screen to detect subjects that may be at a higher risk of developing narrow angle glaucoma, a contraindicated condition to topiramate. 5/30/13
3. Modified the Clinician Administered PTSD Scale (CAPS) to incorporate questions from the original CAPS and the new version, CAPS5. By administering the revised version, we will be able to characterize the study population's PTSD diagnosis as defined by DSM-IV and DSM5. 4/1/13-6/30/13
4. Modified the PTSD Checklist (PCL) to incorporate questions from the original PCL-S and the new version, PCL5. By administering the revised version, we will be able to characterize the study population's PTSD diagnosis as defined by DSM-IV and DSM5. 4/1/13-6/30/13
5. Added additional question to the Structured Clinical Interview for DSM-IV, Substance Used Disorder section (SCID, SUD) so that we may describe the study population's alcohol use disorders in terms of DSM-IV and addictive disorders, as defined by DSM5. 4/1/13-6/30/13

REPORTABLE OUTCOMES: Provide a list of reportable outcomes that have resulted from this research to include: manuscripts, abstracts, presentations; licenses applied for and/or issued; degrees obtained that are supported by this award; development of cell lines, tissue or serum repositories; informatics such as databases and animal models, etc.; funding applied for based on work supported by this award; employment or research opportunities applied for and/or received based on experience/training supported by this award

1. Presented current study and past pilot [W81XWH-05-2-0094] study to the Northern California Institute of Research and Education (NCIRE) Board Members. 2/21/13
2. Published a paper from the pilot [W81XWH-05-2-0094] study in Military Medicine. 6/6/13

   Kalapatapu RK, Delucchi KL, Lasher BA, Vinogradov S, Batki SL. "Alcohol Use Biomarkers Predicting Cognitive Performance: A Secondary Analysis in Veterans with Alcohol Dependence and Posttraumatic Stress Disorder". *Military Medicine*, 178(9), 974-980.
3. Abstract from pilot [W81XWH-05-2-0094] study accepted for presentation at the 2013 Annual Meeting for American Academy of Addiction Psychiatry (AAAP). 8/28/13

   Batki, S.L., Pennington, D.L., Lasher, B.A., Herbst, E., Metzler, T., Delucchi, K., Richards, A. Heinz, A., Neylan, T.C. “Topiramate Effects on Sleep in Veterans with PTSD and Alcohol Dependence: A Pilot Controlled Trial”.
4. Performed preliminary (blinded) analysis of demographics, self-reported drinking, and adverse events in support of the DSMB meeting. [Please see Supporting Data (pg 79)]. 8/31/13
5. Presented study overview & progress and pilot [W81XWH-05-2-0094] study data at MOMRP Substance Abuse IPR in Ft. Detrick, MD. 9/16/13
6. Created 2 databases/interfaces for data collection in real-time. Tasks included the design, development, testing, and validation of activities.
   i. **Qualtrics**, an online user interface was designed to directly collect and store information at the time of study visit. All self-report measures are collected in this format.
   ii. Data gleaned from measures and procedures that are more structured or involved are collected via an **Access** database/interface. Measures such as psychological assessments or procedures such as blood collection are entered in this system.

   All data are stored on a SQL server which resides behind the San Francisco VA Medical Center firewall. 12/1/12 – 9/29/13

CONCLUSION: Summarize the results to include the importance and/or implications of the completed research and when necessary, recommend changes on future work to better address the problem. A "so what section" which evaluates the knowledge as a scientific or medical product shall also be included in the conclusion of the report.

There are no conclusions to draw at this time.

REFERENCES: List all references pertinent to the report using a standard journal format (i.e. format used in *Science, Military Medicine*, etc.).

None at this time.

APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, study questionnaires, and surveys, etc.

TOPIRAMATE EFFECTS ON SLEEP IN VETERANS WITH PTSD AND ALCOHOL DEPENDENCE: A PILOT CONTROLLED TRIAL

Steven L. Batki, M.D. [1,2]; David L. Pennington, Ph.D.[3]; Brooke A. Lasher[3]; Ellen Herbst[1,2], M.D.; Thomas Metzler[3]; Kevin Delucchi, Ph.D.[1]; Anne Richards, M.D. [1,2]; Adrienne Heinz, Ph.D.[4]; Thomas C. Neylan, M.D. [1,2]

[1]UCSF Department of Psychiatry, San Francisco, CA; [2]San Francisco VA Medical Center, [3]Northern California Institute for Research and Education, San Francisco, CA, and [4]Palo Alto VA Health Care System, Menlo Park, CA

Background: Poor sleep quality is associated with heightened PTSD symptom severity and poor treatment outcomes for problematic alcohol use. However, little is known about the effects of topiramate pharmacotherapy on sleep for comorbid PTSD and alcohol dependence (AD). The current investigation sought to examine differences in sleep quality across a 12-week RCT of topiramate vs. placebo.

Methods: We conducted secondary analyses of topiramate vs. placebo in 30 veterans with PTSD/AD. The Pittsburgh Sleep Quality Inventory (PSQI) and the Insomnia Severity Index (ISI) were administered at baseline and throughout the trial to assess sleep quality. Mean/median baseline PSQI and ISI scores were 13.2/14.0 and 17.9/17.0 respectively indicating severely disrupted sleep. We used linear mixed modeling to assess longitudinal change and group differences, covarying for respective baseline scores. Effect sizes (ES) were calculated using average Cohen's d of all cross-sectional post-baseline assessments for each measure.

Results: There were no group-by-time interactions seen on either measure. However, there was a significant main effect for time (p=.020) showing a decrease on PSQI scores and a trend (p=.085) for decrease on ISI scores over the 12-week trial. There were no significant main effects for group on either measure although the topiramate group had numerically lower scores at each post-baseline assessment with moderate effect sizes (PSQI: ES=.44; ISI: ES=.46).
We also conducted exploratory analysis examining specific items from the PSQI and PTSD Symptom Checklist (PCL) related to PTSD sleep symptoms. There were no group-by-time interactions or main effects for time. However, the topiramate group had significantly less trouble sleeping due to bad dreams (PSQI-Item 5h) with a strong effect when compared to the placebo group at post-baseline assessments (p=.017, ES=.91). PCL-Item 2 (disturbing dreams) and 13 (insomnia) were not significant (p>.162) but showed moderate group effects (ES=.45 and .39 respectively).

Conclusions: Involvement in a 12-week RCT of topiramate vs. placebo treatment resulted in decreases in poor sleep quality in those with comorbid PTSD/AD. Topiramate treatment is associated with less trouble sleeping due to bad dreams and may result in better sleep quality overall in this treatment-seeking population. However, due to limited power, a larger trial is warranted to determine clinical significance of topiramate on sleep symptoms in patients with PTSD and AD.

Source of Funding: Department of Defense Grant No: W81XWH-05-2-0094

Alcohol Use Biomarkers Predicting Cognitive Performance: A Secondary Analysis in Veterans With Alcohol Dependence and Posttraumatic Stress Disorder

Raj K. Kalapatapu, MD†; Kevin L. Delucchi, PhD*; Brooke A. Lasher, BA†‡; Sophia Vinogradov, MD*†‡; Steven L. Batki, MD*†‡*

ABSTRACT Objective: We conducted a secondary analysis of baseline data from a recently completed pharmacological pilot clinical trial among 30 veterans with alcohol dependence and posttraumatic stress disorder (PTSD). This trial included baseline measures of alcohol use biomarkers, both indirect (carbohydrate-deficient transferrin, GGT [γ-glutamyltransferase], mean corpuscular volume, AST [aspartate aminotransferase], alanine aminotransferase) and direct (ethyl glucuronide, ethyl sulfate), as well as neurocognitive measures (Trail Making Test parts A and B, Hopkins Verbal Learning Test—Revised, Balloon Analogue Risk Task, Delay Discounting Task). Methods: Two regression models were estimated and tested for each neurocognitive measure (dependent measure). The first model included the alcohol use biomarker alone as the predictor. The second model included the alcohol use biomarker along with the following 3 additional predictors: Beck Depression Inventory, Clinician-Administered PTSD Scale, and receiving medications. Results: In both models, the indirect biomarkers, such as GGT and AST, significantly predicted performance on the Hopkins Verbal Learning Test—Revised %Retention. GGT alone significantly predicted performance on the Trail Making Test part A. Conclusions: Indirect alcohol use biomarkers may have a specific role in identifying those veterans with alcohol dependence and PTSD who have impaired cognitive performance. However, direct alcohol use biomarkers may not share such a role.

INTRODUCTION

Alcohol use disorders are a major public health problem[1] and constitute the most prevalent forms of addiction in veterans.[2] Cognition is a key area of research in the field of alcohol use disorders.[3,4] Cognitive impairment is well-documented in individuals with alcohol use disorders,[5] and alcohol-related clinical outcomes (e.g., abstinence, relapse, treatment completion) are moderated by a range of cognitive impairments.[6–11] Cognition plays an important role in clinical outcomes, yet recognizing and screening for cognitive impairment in addiction populations remains uncertain and difficult.[12–16] A comprehensive neurocognitive evaluation may not be routinely feasible in addiction settings, as these evaluations are often time intensive and resource consuming.[16–18] When managing veterans with alcohol use disorders, quicker adjunctive tools that clinicians could use to screen for those individuals at higher risk of cognitive impairment are needed.

One potential tool that may fulfill this role is the alcohol use biomarker. Alcohol use biomarkers are broadly divided into indirect and direct biomarkers.[19,20] The indirect biomarkers include aspartate aminotransferase (AST), alanine aminotransferase (ALT), mean corpuscular volume (MCV), γ-glutamyltransferase (GGT), and carbohydrate-deficient transferrin (CDT). The direct biomarkers include ethyl glucuronide (EtG), ethyl sulfate (EtS), and phosphatidylethanol. Past research has shown that several indirect alcohol use biomarkers are correlated with cognitive performance in individuals with alcohol use disorders: AST,[21] ALT,[22] MCV,[23] and GGT.[24–29] Thus, alcohol use biomarkers may not only be used to screen for alcohol problems or abstinence,[19] but also have a specific role in screening for cognitive impairment in individuals with alcohol use disorders. These biomarkers may offer more than simply getting a history of the amount and frequency of recent alcohol use.

Though several indirect biomarkers have been explored with respect to cognitive performance, the newer direct biomarkers, such as EtG and EtS, have not received any attention in the literature. Although the direct biomarkers are minor metabolites of alcohol,[30] these biomarkers, such as EtG, can also be found in the brain.[31] Whether any of the direct biomarkers are associated with cognitive performance in individuals with alcohol use disorders remains an open question.

In an effort to add to this scarce literature on the association of alcohol use biomarkers and cognitive performance, we conducted a secondary analysis of baseline data from

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Dr. Kalapatapu completed the background literature search and completed the statistical analyses (with guidance from Dr. Delucchi). Dr. Kalapatapu wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

The authors report no conflicts of interest. The authors alone are responsible for the content, the study design, protocol implementation, statistical analysis, interpretation of results, manuscript preparation, and decision to submit the manuscript for publication. The views expressed in this article are those of the authors and do not necessarily represent the official views of the NIH.

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a recently completed pharmacological pilot clinical trial among veterans with alcohol dependence and posttraumatic stress disorder (PTSD). This study included the measures, at baseline, of indirect (CDT, GGT, MCV, AST, ALT) and direct (EtG, EtS) alcohol use biomarkers and neurocognitive measures, which allowed us to explore the relationship between biomarkers and cognitive performance.

Because this study was conducted in alcohol-dependent veterans with comorbid PTSD, we were also able to explore the unique relationship between alcohol use biomarkers and cognitive performance in a group having particularly poor clinical outcomes.[32–35] To the best of our knowledge, the relationship between alcohol use biomarkers and cognitive performance specifically in veterans with alcohol dependence and PTSD has not been previously explored.

In this sample of veterans with alcohol dependence and PTSD, we hypothesized that the indirect biomarkers would predict baseline cognitive performance. On the basis of the evidence that they can be found in the brain, we also hypothesized that the direct biomarkers would predict baseline cognitive performance.

METHODS

Study Setting

Full details of the study used for this analysis can be found on Clinicaltrials.gov (identifier no. NCT01087736), titled "Topiramate Treatment of Alcohol Use Disorders in Veterans With Post Traumatic Stress Disorder (PTSD): A Pilot Controlled Trial of Augmentation Therapy". Briefly, this two-armed double-blind randomized controlled pilot study enrolled 30 veteran participants with alcohol dependence and PTSD. Participants met *Diagnostic and Statistical Manual of Mental Disorders*, 4th Ed, Text Revision (DSM-IV-TR) criteria for current alcohol dependence and for "heavy drinking" in the past 30 days before screening. For men, "heavy drinking" was defined as, on average, drinking more than 15 standard drinks per week. For women, "heavy drinking" was defined as, on average, drinking more than 8 standard drinks per week.[36] The 12-week double-blind treatment phase consisted of randomly assigning participants to either topiramate or placebo. Participants also received weekly manualized alcohol counseling[37] and standard PTSD treatment.

All research activities were conducted at the San Francisco Veterans Affairs Medical Center (SFVAMC). All participants provided informed consent. The study was approved by the Committee on Human Research at the University of California, San Francisco; the Research and Development Committee at the SFVAMC; and the U.S. Army Medical Research and Materiel Command Human Research Protection Office.

Measures

Demographic data, such as age, sex, race, ethnicity, years of education, marital status, and occupational status, were collected. Psychiatric diagnoses and concurrent medication use were captured by a review of each participant's electronic medical record at the SFVAMC. Substance use disorder diagnoses were assessed using the Substance Use Disorders module of the Structured Clinical Interview for DSM-IV-TR, Research Version, Patient Edition (SCID-I/P).[38] The level of substance use for the past 90 days was assessed using the Timeline Followback Method.[39] PTSD was diagnosed by the Clinician-Administered PTSD Scale.[40] The level of depression was assessed using the 21-item self-report Beck Depression Inventory.[41]

Blood samples were obtained for CDT (specifically serum %disialo-CDT), GGT, MCV, AST, and ALT levels. Urine samples were obtained for EtG and EtS levels. Standard operating procedures were followed by the Clinical and Translational Science Institute at the SFVAMC to obtain these samples. Levels of GGT, MCV, AST, and ALT were analyzed locally at the SFVAMC Department of Laboratory Medicine. CDT sample was shipped and analyzed at the Clinical Neurobiology Laboratory in the Institute of Psychiatry at the Medical University of South Carolina. EtG and EtS samples were shipped and analyzed at the Department of Laboratory Medicine at the Yale University School of Medicine.

The Trail Making Test (TMT) part A was used to assess psychomotor speed and simple visual attention and part B was used to assess task switching and cognitive flexibility; the raw scores were converted to *T* scores.[42] The Hopkins Verbal Learning Test—Revised (HVLT-R) was used to assess verbal memory.[43] We used the %retention score for this analysis, where the raw score was converted to a *T* score; the assessment of retention is relatively free of effortful memory search and retrieval.[43] The Balloon Analogue Risk Task (BART) was used to assess risk taking[44]; we used the primary score of "adjusted average number of pumps on unexploded balloons." The Delay Discounting (DD) Task was used to assess impulsivity[45]; we used the Kln score, defined as the log-transformed DD after applying the hyperbolic function.

Statistical Analysis

All analyses were conducted using IBM SPSS Statistics, version 20 (Armonk, New York). All continuous variables were checked for normality (Kolmogorov–Smirnov and Shapiro–Wilk tests), and nonparametric tests were used when appropriate. All continuous variables were also checked for extreme values; values with a z-score > 3.29 or < -3.29 were adjusted to the next highest value. Where adjusted results differed from the original data, the adjusted results are presented. Because most values were undetectable at <100 ng/mL, EtG was dichotomized into <100 ng/mL vs. >100 ng/mL. Because most values were undetectable at <50 ng/mL, EtS was dichotomized into <50 vs. >50 ng/mL.

Two multiple regression models were estimated and tested for each neurocognitive measure (dependent measure). The

first model included the alcohol use biomarker alone as the predictor. The second model included the alcohol use biomarker along with the following 3 additional predictors: Beck Depression Inventory (Total score), Clinician-Administered PTSD Scale (Severity score), and receiving medications (PTSD, substance use disorder, or other psychiatric medications). As mood symptoms,[46] PTSD symptoms,[47] and medications[48] can affect cognitive performance, we included these 3 additional predictors in the second model to determine if they would make a significant contribution.

Because this was an exploratory secondary analysis, we did not control for type I error; p-values < 0.05 were considered statistically significant. Assumptions in each regression model were checked by assessing several parameters[49] such as Durbin–Watson statistic (close to 2 and not <1 or >3), collinearity (Tolerance and Variance Inflation Factor close to 1), standardized residuals (not >3), Cook's distance (not >1), linearity/homoscedasticity (plots of *ZRESID against *ZPRED randomly and evenly dispersed), and normality of residuals (normal histograms and normal probability plots with data points near the line). All of these assumptions in each multiple regression model for each neurocognitive measure were met.

TABLE I. Baseline Demographic and Clinical Data

	Mean (SD[a]), Median (Range, IQR[b]), or %
Age	55 (25–65, 20)
Male	93.30%
Caucasian	53.30%
African American	26.70%
Hispanic	10.00%
Years of Education	14 (7–18, 2)
Married	26.70%
Unemployed	36.70%
Major Depressive Disorder	13.30%
Any Type of Bipolar Disorder	3.30%
Generalized Anxiety Disorder	3.30%
Panic Disorder	3.30%
Obsessive-Compulsive Disorder	3.30%
Cannabis Abuse or Dependence	6.70%
Cocaine Abuse or Dependence	16.70%
Sedative Abuse or Dependence	6.70%
Opiate Abuse or Dependence	3.30%
Receiving Medications for PTSD	46.70%
Receiving Medications for a Substance Use Disorder	6.70%
Receiving Other Psychiatric Medications	60.00%
Beck Depression Inventory: Total Score[c]	24.9 (11.9)
Clinician-Administered PTSD Scale: Intensity Score	39.4 (8.3)
Clinician-Administered PTSD Scale: Frequency Score	38.9 (9.3)
Clinician-Administered PTSD Scale: Severity Score	78.3 (16.6)

n = 30 except where noted. [a]SD = standard deviation. [b]IQR = interquartile range. [c]n = 29 because of 1 missing data point.

TABLE II. Baseline Substance Use, Alcohol Use Biomarker, and Neurocognitive Data

	Mean (SD), Median (Range, IQR), or %
Baseline Drinking Severity	
No. of Drinks in the Past 30 Days	183 (68–637, 158)
No. of Drinking Days in the Past 30 Days	22.5 (5–30, 19)
No. of Drinks Per Drinking Day in the Past 30 Days	9.5 (3.6–27.2, 7.4)
No. of Heavy Drinking Days in the Past 30 Days	14.5 (0–30, 19)
No. of Days of Cannabis Use in the Past 90 Days [n = 9]	45 (9–90, 78)
No. of Days of Cocaine Use in the Past 90 Days [n = 3]	37.0 (45.9)
No. of Days of Opiate Use in the Past 90 Days [n = 1]	1
No. of Cigarettes Used in the Past 90 Days [n = 13]	1,075.5 (648.9)
EtG[a,b] (>100 ng/mL)	30%
EtS[a,c] (>50 ng/mL)	37%
CDT[d]	1.7% (0.9–5.0, 1.05)
GGT	47.5 (16–722, 52)
MCV	96.2 (69.9–103.6, 8.5)
AST	35.5 (17–174, 32.8)
ALT	38 (18–106, 49)
HVLT-R	
%Retention T Score	55 (25–80, 11)
BART	
Adjusted Average Number of Pumps on Unexploded Balloons[e]	35.9 (15.4)
DD	
Kln[e,f]	−5.4 (2.0)
TMT-A	
T Score	44.9 (11.6)
TMT-B	
T Score	45.6 (11.0)

n = 30 except where noted. [a]n = 27 because of 3 missing data points. [b]Because most values were undetectable at <100 ng/mL, EtG was dichotomized into <100 vs. >100 ng/mL. [c]Because most values were undetectable at <50 ng/mL, EtS was dichotomized into <50 vs. >50 ng/mL. [d]n = 29 because of 1 missing data point. Values represent serum %disialo-CDT. [e]n = 28 because of 2 missing data points. [f]Kln = log-transformed delay discounting after applying the hyperbolic function.

Finally, previous evidence shows that alcohol intake itself can affect cognitive performance.[5] We explored whether the number of drinks significantly correlated (Pearson's correlation) with any of the neurocognitive measures.

RESULTS

Table I presents baseline demographic and clinical data. Table II presents baseline substance use, alcohol use biomarker, and neurocognitive data. Tables III and IV present the multiple regression analyses between alcohol use biomarker data and neurocognitive data. Table III presents the results with the first model that included the alcohol use biomarker alone as the predictor; Table IV presents the

TABLE III. Multiple Regression Analyses Between Alcohol Use Biomarker Data and Neurocognitive Data (Dependent Measure)

	HVLT-R: %Retention *T* Score	BART: Adjusted Average Number of Pumps on Unexploded Balloons	DD: Kln	TMT-A: *T* Score	TMT-B: *T* Score
EtG	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
EtS	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
CDT	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
GGT	$F(1,27) = 7.27$, $p = 0.01$, $R^2 = 0.21$, $\beta = 0.46$[a]	$p > 0.10$	$p > 0.10$	$F(1,27) = 5.12$, $p = 0.032$, $R^2 = 0.16$, $\beta = -0.40$[b]	$p > 0.10$
MCV	$p > 0.10$	$F(1,25) = 3.01$, $p = 0.095$, $R^2 = 0.11$, $\beta = 0.33$	$p > 0.10$	$p > 0.10$	$p > 0.10$
AST	$F(1,27) = 6.53$, $p = 0.017$, $R^2 = 0.20$, $\beta = 0.44$[b]	$p > 0.10$	$p > 0.10$	$F(1,27) = 3.50$, $p = 0.072$, $R^2 = 0.12$, $\beta = -0.34$[b]	$p > 0.10$
ALT	$p > 0.10$	$p > 0.10$	$p > 0.10$	$F(1,27) = 4.12$, $p = 0.052$, $R^2 = 0.13$, $\beta = -0.36$	$p > 0.10$

Alcohol use biomarker alone as the predictor. [a]Correction for extreme values did not change results, so original results are presented. [b]Correction for extreme values changed results, so corrected results are presented.

TABLE IV. Multiple Regression Analyses Between Alcohol Use Biomarker Data and Neurocognitive Data (Dependent Measure)

	HVLT-R: %Retention *T* Score	BART: Adjusted Average Number of Pumps on Unexploded Balloons	DD: Kln	TMT-A: *T* Score	TMT-B: *T* Score
EtG	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
EtS	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
CDT	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
GGT	$F(4,24) = 4.70$, $p = 0.006$, $R^2 = 0.44$ GGT $\beta = 0.64$[a], $p = 0.001$ [1] $\beta = -0.36$, $p = 0.045$ [2] $\beta = 0.47$, $p = 0.01$ [3] $\beta = 0.29$, $p = 0.095$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
MCV	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
AST	$F(4,24) = 2.94$, $p = 0.041$, $R^2 = 0.33$ AST $\beta = 0.49$[b], $p = 0.01$ [1] $\beta = -0.27$, $p = 0.16$ [2] $\beta = 0.36$, $p = 0.06$ [3] $\beta = 0.17$, $p = 0.33$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$
ALT	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$	$p > 0.10$

Alcohol use biomarker plus 3 predictors: (1) Beck Depression Inventory (Total score), (2) Clinician-Administered PTSD Scale (Severity score), and (3) receiving medications (PTSD, substance use disorder, or other psychiatric medications). Significant and approaching significance results are reported. [a]Correction for extreme values did not change results, so original results are presented. [b]Correction for extreme values changed results, so corrected results are presented.

results with the second model that included the alcohol use biomarker along with the 3 additional predictors (Beck Depression Inventory [Total score], Clinician-Administered PTSD Scale [Severity score], receiving medications [PTSD, substance use disorder, or other psychiatric medications]).

CDT did not significantly predict performance on any neurocognitive measure. In both models, GGT significantly predicted performance on the HVLT-R %Retention; the Beck Depression Inventory (Total score) and the Clinician-Administered PTSD Scale (Severity score) also significantly contributed to the second model along with GGT. In only the first model, GGT significantly predicted performance on the TMT-A. GGT did not significantly predict performance on the BART, DD, TMT-B, and in the second model on the TMT-A.

In only the first model, MCV predicting performance on the BART approached significance. It did not significantly predict performance on any other neurocognitive measure.

In both models, AST significantly predicted performance on the HVLT-R %Retention. In only the first model, AST predicting performance on the TMT-A approached significance. AST did not significantly predict performance on the BART, DD, TMT-B, and in the second model on the TMT-A.

In the first model, ALT predicting performance on the TMT-A approached significance. It did not significantly predict performance on any other neurocognitive measure. EtG and EtS did not significantly predict performance on any neurocognitive measure.

The number of drinks did not significantly correlate with any of the neurocognitive measures (all p's > 0.05). These

results were nonsignificant for the number of drinks in the past 4 to 90 days. Also, because GGT and AST were the only two measures to predict performance on the HVLT-R %Retention, we assessed whether these were correlated; GGT and AST were correlated in this analysis ($r = 0.74$, $p < 0.001$).

DISCUSSION

Baseline alcohol use biomarker and neurocognitive data from a pilot clinical trial among veterans with alcohol dependence and PTSD were analyzed in this secondary analysis. GGT and AST significantly predicted performance on the HVLT-R %Retention; the Beck Depression Inventory (Total score) and the Clinician-Administered PTSD Scale (Severity score) also significantly contributed to predicting performance on the HVLT-R %Retention along with GGT. GGT alone, without any other predictors, significantly predicted performance on TMT-A. Without any other predictors, AST and ALT alone predicting performance on the TMT-A approached significance. Without any other predictors, MCV alone predicting performance on the BART approached significance. Thus, the initial hypotheses were partially supported.

The indirect biomarkers may predict neurocognitive performance for several reasons such as (1) by serving as a surrogate marker for heavy alcohol use, thereby representing alcohol's potential for direct neurotoxicity; (2) by serving as a marker of hepatic dysfunction for transaminases, thereby representing hepatic effects on brain function; and (3) by having a direct neurotoxic effect of their own. The finding that GGT and AST predicted performance on some neurocognitive measures is consistent with that of previous research.[21,24–29] For example, increases in GGT may increase the transport of amino acids into the brain across the blood–brain barrier, which may alter cognitive performance.[24] GGT has also been associated with gray matter decline[50] and brain shrinkage,[51] which may affect cognitive performance. GGT is known to be a marker of oxidative stress and has been found to be elevated in patients with Alzheimer's disease,[52] which highlights a potential association of GGT with cognitive performance. Cognitive changes because of poor liver function may be due to the liver failing to catabolize circulating neurotoxins,[53] and GGT and AST may help identify patients who show a change in visual attention and verbal memory performance.

ALT significantly predicted performance on the TMT-A, but the limitations of the sample might have contributed to ALT not fully achieving significance. Approaching significance, the MCV predicting BART performance is interesting.Though MCV may appear to be unrelated to cognition, some studies have shown that erythrocyte volume may influence cognition,[54] and that MCV can predict delirium after surgery.[23] MCV has also been associated with gray matter decline[50] and ventricular enlargement.[55] One possibility is that the increased erythrocyte volume, which is found in alcohol dependence[19] and during times of stress,[56,57] may lead to erythrocytes having difficulty passing through narrow brain capillaries and subsequently affecting cognitive performance.[54]

CDT not predicting performance on any neurocognitive measure is consistent with previous reports.[25] It is important to note that other studies in individuals with alcohol use disorders have similarly shown no association of indirect biomarkers with any neurocognitive measure.[58,59] One plausible explanation for this is that because the direct biomarkers are minor metabolites of alcohol,[30] the concentrations of these biomarkers in the brain may not have been sufficient to affect the neural pathways underlying cognitive performance. Another plausible explanation may be that the direct biomarkers represent alcohol use for a much briefer time than the indirect markers, which represents anywhere from several weeks (GGT, AST, ALT) to several months (MCV)[19]; therefore, the indirect biomarkers represent more chronic measures of heavy drinking and more likely represent the direct toxic effects of alcohol on brain function.

This analysis suggests that in addiction settings, some of the indirect alcohol use biomarkers serve as an indicator of a subset of patients who are at high risk for cognitive impairment. Alcohol use biomarkers cannot replace a comprehensive neurocognitive evaluation for assessing cognitive impairment. Rather, in settings where a comprehensive neurocognitive evaluation is not feasible, alcohol use biomarkers might be the next best tool that clinicians could potentially use to identify veterans with alcohol dependence and PTSD who are likely to show cognitive impairment. Cost and practicality of ordering alcohol use biomarkers would be some hurdles for a clinician to implement these biomarkers in routine clinical practice. For example, in our own San Francisco Veterans Affairs clinical setting, the two indirect biomarkers (GGT, AST) in this analysis that predicted cognitive performance can more easily be ordered through our computerized medical record system, compared to the direct biomarkers that require special ordering and processing. Thus, in addition to the scientific relationship between alcohol use biomarkers and cognitive performance, clinicians must consider cost and practicality of ordering alcohol use biomarkers when implementing these biomarkers in routine clinical practice.

This analysis has several strengths. First, seven alcohol use biomarkers were analyzed. Second, three additional predictors were integrated into the second regression model and yet still found significance with a few biomarkers. Third, a naturalistic sample of veterans was analyzed, which can help generalize these findings to veterans with alcohol dependence and comorbid PTSD. Finally, this is the first known analysis to explore the relationship between alcohol use biomarkers and cognitive performance in veterans with both alcohol dependence and PTSD.

Inevitably, this analysis also has limitations. First, the study was not specifically designed to assess the aims of this post hoc analysis. As a result, the number of exploratory analyses conducted (Tables III and IV) likely produced some type I errors. Second, because the sample size was small, this may have been the reason for only obtaining approaching significance level findings for some biomarkers. A larger sample size can help clarify the results. Third, because the sample was naturalistic and included veterans with other comorbid non-PTSD and non-alcohol use disorders and concurrent medication use (Table I), such broad inclusion/exclusion criteria may have contributed to some of the nonsignificant findings given in Tables III and IV. A future study with more stringent delineation of primary psychiatric disorder, substance use disorder, and medication use criteria may help clarify the relationship between alcohol use biomarkers and cognitive performance in veterans specifically with alcohol dependence and PTSD.

Fourth, because most EtG and EtS values were undetectable, dichotomizing the continuous variables of EtG and EtS most likely resulted in a loss of statistical power.[60–62] As a result, the nonsignificant results for EtG and EtS (Tables III and IV) may have been due to a "floor effect." A future study with more accurate EtG and EtS detection at levels below the current threshold can help maintain these variables as continuous when conducting data analyses. Finally, a more comprehensive neurocognitive battery evaluating other cognitive domains (e.g., visuospatial memory, attentional bias, and executive function) may add further information on the relationship between alcohol use biomarkers and other cognitive domains.

CONCLUSIONS

This analysis of alcohol use biomarkers and cognitive performance in a pilot clinical trial among veterans with alcohol dependence and PTSD found that indirect biomarkers, such as GGT and AST, may have a specific role in identifying those veterans who show a change in visual attention and verbal memory performance. However, direct biomarkers may not have a similar role. Future directions to confirm or refute these findings include the use of a larger sample size, a more comprehensive neurocognitive battery, and recruiting a sample with more stringent inclusion/exclusion criteria.

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Subject # _____-☐☐☐-☐☐ Week ☐☐ Date☐☐ /☐☐ /☐☐

MEDICAL MANAGEMENT

Follow-up Session

Medical Manager Checklist:

Review:	*Complete:*
☐ Lab results, vital signs and other patient information	☐ Medication Compliance Worksheet
☐ Drinking patterns as determined by TLFB	☐ Suicide Risk Assessment
☐ New AEs and Changes to Concom Meds	☐ CPRS Study Note
☐	☐
☐	☐

1. Review blood pressure reading, liver enzymes, any abnormal lab values, other drinking related medical symptoms.	**2. State your medical opinion of how alcohol is affecting the patient physically. Tie results and symptoms to heavy alcohol use.**
Vital Signs: **Normal Range:** **Blood pressure:** _____ / _____ 90/49 – 149/99 **Pulse:** _____ 50 - 99 **Liver function test results:** **Normal Range:** AST (SGOT): _____ **AST (SGOT):** 11 IU/L to 47 IU/L ALT (SGPT): _____ **ALT (SGPT):** 7 IU/L to 53 IU/L GGT : _____ **GGT**: **M** 9-50 units/L **F** 8-40 units/L MCV: _____ **MCV:** 80 - 100 fl **Other medical conditions affected by drinking and relevant lab results:** ☐Diabetes ☐Heart disease ☐GI:_____ ☐Insomnia ☐Depression ☐Anxiety ☐Pain ☐Other:_____	**If blood pressure is elevated, describe relationship between high blood pressure and heavy drinking.** **Describe relationship between conditions and heavy drinking, including relevant lab results.** **Observations of patient cognition:** Mood: Physical signs: Other:

3. Review concomitant medications and adverse events. Administer Suicide Risk Assessment via CPRS.	
Emergent AEs and New Concom Meds: **Comments:**	**"Any other side effects or medications not already mentioned?"**

4. Inquire about general progress and patient concerns since last visit:	
Drinking Status → from TLFB **Date of last drink: _____** **Since the last visit:** **How many drinking days (any alcohol):** _____ days in the past _____ days **How many heavy drinking days (M: 5+ drinks/day, F: 4+ drinks/day):** _____ days in the past _____ days **Comments:**	**"How have you been since our last visit?"** **"What was difficult?"** **"What went well?"** **"How were you able to keep from drinking?"** • **If patient did drink →** "What were the circumstances? Remember, change occurs in small steps; keep trying don't get discouraged" **"How great was your desire to drink?"** • **Patient did drink but found desire diminished** "Reductions in your desire to drink may be the first sign to change for you." • **Patient's desire to drink strong** "Congratulations on choosing not to drink when you really wanted to. You have taken an important step toward recovery!" **If patient continued with abstinence** • "Congratulations for staying abstinent. You are demonstrating your determination to change. You are making great progress toward your recovery!"

5. Other treatment received		
Yes	No	
☐	☐	Started any new medications? (specify) _____
☐	☐	Attended mutual support groups? If yes, how often? _____
☐	☐	Received alcohol or addiction counseling? (specify)_____
☐	☐	Received other counseling? (specify) _____
☐	☐	Entered a treatment program? ☐Residential ☐intensive outpatient ☐other (specify) _____
☐	☐	Been hospitalized for alcohol or drug use? (specify) _____
☐	☐	Been treated for withdrawal (shakes)? (specify)_____

6. Assess medication compliance and determine what treatment scenario is applicable and complete visit based upon applicable scenario.	7. Inquire about any skipped doses. Query relation of skipped doses to drinking.
Since the last visit, how many days has the patient taken medication? (1) # of pills presumed to have been taken (1i from Med Dispense form): _____ (2) # of pills expected to have been taken since last visit (1f from Med Dispense form): _____ % adherence: _____ (divide ½) **Comments**:	**What is the patient's perception of the medication's effectiveness:** ☐ Helpful ☐ Not helpful ☐ Not sure ☐ Specify: _____ ☐ Abstinent/Medication Compliant ☐ Abstinent/non-compliant ☐ Non-abstinent/medication compliant ☐ Non-abstinent/non-compliant

Abstinent & Medication Compliant	
Comments:	-Reinforce the patient's ability to follow advice and stick to the plan. Praise progress. Ask how patient did it. - Remind patient it is necessary to continue to take all medication and attend session until end of study. -Review benefits of abstinence and medication in general terms (improved health, fewer drinking related problems -Provide support -Reinforce AA or other support group attendance -Conclude on a positive note with general encouragement and praise –"Sounds like things are going well. Keep up the good work!"

Abstinent & Non-compliant	
Comments:	- Congratulate the patient for not drinking. -Review the general benefits of abstinence and how medications help abstinence -Ask why the medications are not taken regularly – problem solve. This is something you can help the patient change, such as if noncompliance is related to side effects. -Tell the patient that he/she may significantly improve his/her chances for sustained improvement by taking the medications. -Revise/reconstruct medication (non) compliance checklist if necessary -Reinforce AA or other support group attendance -Conclude on a positive note with general encouragement and praise

Non-abstinent & Medication Compliant	
Comments:	-Reinforce patient for taking medication -Remind patient of why she/he sought treatment -Praise any small steps toward abstinence (e.g., fewer heavy drinking days) Reassure your patient that recovery is a gradual process and that occasional returns to drinking sometimes occur along the way. -Review the benefits of abstinence -Complete medication compliance checklist. -If during dose titration remind patient that medication is not yet up to full dosage. Remind patient that medications take time to work and may not have begun to yield their full effect on reducing drinking. -If patient appeals to you for advice on how to become abstinent, find out if he/she has been drinking at home or at a bar or another regular place. If at home, encourage the patient to get the alcohol out of the house. If at a bar or with

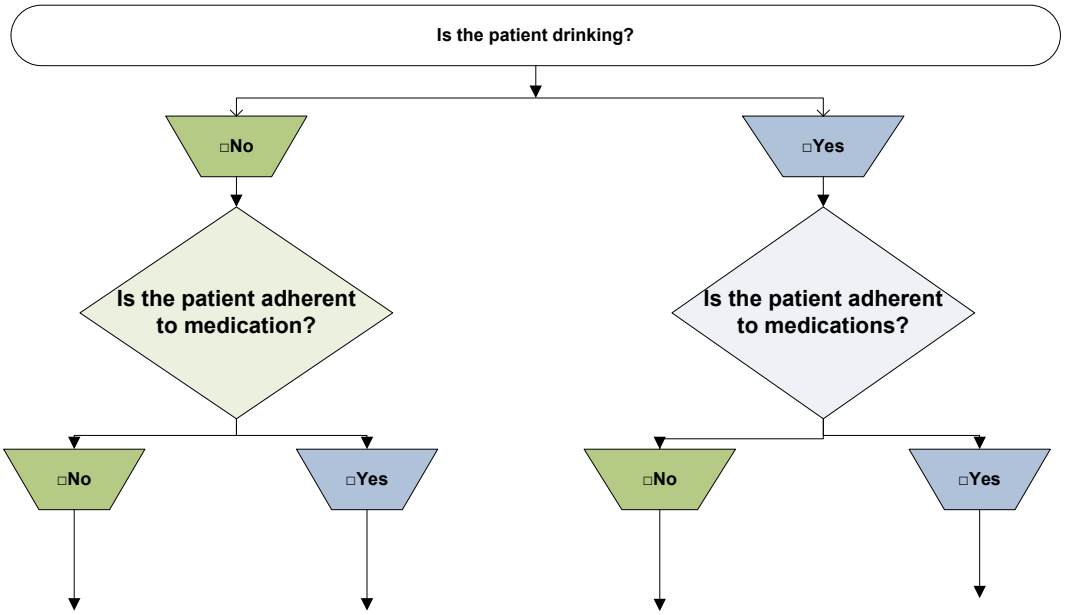
	specific people, suggest not associating with drinking buddies and not going to bars. - Ask if there is a particular time of the day that the patient drinks. If so, suggest that he/she find some other activity to distract him/her at that time. -Review the benefits of mutual support group meetings. -Conclude on a positive note with general encouragement and praise

Non-abstinent & Non-compliant	
Comments:	-Reinforce patient for any progress you see (including coming in for a session) -Review the initial reasons for seeking treatment (i.e., negative consequences of drinking) -Review the benefits of abstinence. Encourage the patient to give abstinence a chance. Say that you know that beginning the process of abstaining from alcohol is the most difficult time but if he/she can get the process started, it should get easier as time goes by. -Encourage patient to give treatment a chance. Explain that although it is very difficult to give up drinking, it is a lot easier to routinely take medications as prescribed. To this end, go over the following. • Briefly evaluate reasons that the patient failed to comply with taking meds. • Review the common reasons why people fail to regularly take their medications • Reconstruct Med Compliance Plan with patient and add new ways to circumvent obstacles to med. compliance. -If patient is no longer motivated to stop or reduce drinking, then: • Remind of reasons for stopping • Remind of benefits of abstinence • Discuss AA attendance • Discuss aspects of treatment that might help increase abstinence -Reinforce AA or other support group attendance. -Conclude on a positive note with general encouragement and praise.

PUT STUDY NOTE IN CPRS:
Select New note
Select New visit
Click on "Historical Visit"
Visit location: RESEARCH-BHC SAP BATKI
Progress Note title: TAP2 < RESEARCH NOTE (TAP2) ALCOHOL PTSD STUDY
Identify Steve as Additional Signer

NEXT APPT DATE & TIME: _____

Clinician's Signature: _____ **Date:** ___ ___ / ___ ___ / ___ ___



□Reinforce participant for remaining abstinent

□Review the general benefits of abstinence and how medications help abstinence.

□Ask why the medications are not taken regularly- problem solve

□Complete medication (non) compliance checklist
a. Review common reasons for non compliance
b. reconstruct medication compliance plan (as needed)

Reinforce/inquire about AA or other support group attendance

Conclude on a positive note with general encouragement and praise.

□Set the next appointment

□Reinforce the patient's ability to follow advice and stick to the plan. Praise progress. Ask how patient did it.

□Remind patient it is necessary to continue to take all medication and attend session until end of study

□Review benefits of abstinence

□Complete medication compliance checklist

Provide support

Reinforce or inquire about AA or other support group attendance

Conclude on a positive note with general encouragement and praise.

□Set the next appointment

Reinforce patient for any progress you see (including coming in for a session)

□Review the initial reasons for seeking treatment (i.e., negative consequences of drinking)

□Review the benefits of abstinence and pharmacotherapy

□Review the reasons for medication nonadherence

Encourage – "give treatment a chance"

□Complete medication (non) compliance checklist.
a. review common reasons for non-compliance
b. addressing barriers to treatment and providing suggestions on minimizing drinking cues
c. reconstruct medication compliance plan (as needed)

If patient is no longer motivated to stop or reduce drinking, then:
a. remind of reasons for stopping
b. remind of benefits of abstinence
c. discuss AA attendance
d. discuss aspects of treatment that might help increase abstinence

Reinforce/inquire about AA or other support group attendance.

Conclude on a positive note with general encouragement and praise

□Set the next appointment

Reinforce patient for taking medication

Remind patient of why she/he sought treatment.

□Praise any small steps toward abstinence (e.g., fewer heavy drinking days)

□Review the benefits of abstinence

Complete medication compliance checklist.

If during dose titration remind patient that medication is not yet up to full dosage.

□Remind the patient that medications take time to work

□Review the benefits of mutual support group meetings

Conclude on a positive note with general encouragement and praise

□Set the next appointment

Clinician Administered Brief Glaucoma (narrow angle closure) Risk Screener

UCSF/SFVAMC --- PI: S. Batki

Subject # _____-☐☐☐-☐☐ Week ☐☐ Date☐☐ /☐☐ /☐☐

*****SOP for referring subject to ophthalmology for glaucoma consult**:
If over 40, and haven't had a glaucoma screen in the past 4 years→ refer to ophthalmology for consult
If answer yes to #2, 4, or 6 → refer to ophthalmology for consult
If answers yes to ≥2 or more of the following #1, 3, 7 → refer to ophthalmology for consult

Please answer the following questions.	YES	NO
1. How old are you? _____ Mark yes if over 40 years old.		
2. Are you from Inuit or Asian decent?		
3. Gender _____ Is the participant female?		
4. Has anyone in your family been diagnosed with Glaucoma? If yes, which family member(s)? _____		
5. 5.a.) Have you had an eye exam within the last four years which included the use of a numbing eye drop and pressure against your eye? (Either in the form of a puff of air or pressure stick)		
5.b.) **If Yes**, when? _____	N/A	N/A
5.c.) **If Yes**, what was the outcome of this test?_____	N/A	N/A
6. Have you ever been diagnosed with Pseudoexfoliation syndrome?		
7. Are you farsighted?		
8. 8.a.)Are you currently taking any over the counter medications such as:		
Decongestants (Sudafed, Mucinex, Tylenol Sinus, etc.)		
Motion Sickness Meds (Dramamine, Benadryl, Bonine, Etc.)		
8.b.)Are you currently prescribed any:		
Adrenergic Agents (Albuterol, Dobutamine, Isoproteranol, Phenylephrine, Metaraminol, etc)		
Antipsychotic Meds (Check CPRS)		
Antidepressants Meds (Check CPRS)		
Anticholinergics (Check CPRS)		
Answered Yes to any of the above medications?		
9. Have you ever had an eye trauma/injury?		

TOTAL Glaucoma Risk Factors Endorsed (highlighted Yellow): _____

Did the research team discuss this participant?	**YES NO**	**Date:_____**
Was the participant given an ophthalmology consult? **Comments:**	**YES NO**	**Date:_____**

******SOP for Post-Tonometry Appointment:**

- 2 Study Physicians to review the outcome of tonometry appointment and determine if subject should remain in study.
- If cannot resolve bw 2 physicians, bring in a 3rd.
- If still no resolution, consult Research Monitor.
- Once determined, Ellen to document outcome in CPRS and Study Coordinator to print-out a copy of the note and place in study binder.

Did a study physician enter note in CPRS documenting outcome of tonometry and if subject safe to participate in study?	**YES NO**	**Date:_____**
Did coordinator print out a copy of note from CPRS	**YES NO**	**Date:_____**

SUPPLEMENTAL INFORMATION

Glaucoma Testing Recommendations:

- Recommend testing before age 40- every two to four years
- from age 40 to age 54- every one to three years
- from age 55 to 64- every one to two years
- after age 65- every six to 12 months

COMMON ADRENERGIC AMINES:

- Albuterol (Alupent, Ventolin, others): given by mouth or as a nasal spray to improve breathing.
- Dobutamine (Dobutrex and generic forms): used to stimulate the heart during surgery or after a heart attack or cardiac arrest.
- Dopamine (Intropin): used to increase cardiac output, blood pressure, and urine flow in treating patients with shock.
- Epinephrine (Adrenalin): used locally to control bleeding from arterioles and capillaries during surgery. It is used to treat shock, as a heart stimulant, and as a decongestant. Epinephrine may be added to local anesthetics to keep the anesthetic in the area where it is applied. Epinephrine may also be applied to the eye to reduce the symptoms of conjunctivitis (red eye).
- Isoproteranol: most widely used to ease breathing problems in asthma and COPD, but also used to control several types of irregular heartbeat until a pacemaker can be implanted.
- Phenylephrine (Neo-Synephrine): used to treat shock and low blood pressure; also used in the form of nose drops or spray to relieve nasal congestion from colds and allergies.
- Metaraminol (Aramine): used to raise the blood pressure and stimulate the heart in treating patients with shock.
- Norepinephrine (Levophed): used to increase the output of the heart and raise blood pressure as part of the treatment of shock.

COMMON ANTICHOLINERGICS:

- **Anti-Muscarinic agents**
  - Benztropine (Cogentin)
  - Ipratropium (Atrovent)
  - Oxitropium (Oxivent)
  - Tiotropium (Spiriva)
  - Glycopyrrolate (Robinul)
  - Oxybutynin (Ditropan, Driptane, Lyrinel XL)
  - Tolterodine (Detrol, Detrusitol)
  - Chlorphenamine (Chlor-Trimeton)
  - Diphenhydramine (Benadryl, Sominex, Advil PM, etc.)
  - Dimenhydrinate (Dramamine)
  - Orphenadrine
  - Trihexyphenidyl
  - Dicyclomine (Dicycloverine)
- **Anti-Nicotinic agents**
  - Bupropion (Zyban, Wellbutrin) - Ganglion blocker
  - Hexamethonium - Ganglion blocker
  - Tubocurarine - Nondeplorizing skeletal muscular relaxant
  - Dextromethorphan - Cough suppressant and ganglion blocker
  - Mecamylamine - Ganglion blocker
  - Doxacurium - Nondeplorizing skeletal muscular relaxant

SOURCE DOC CITATION:

Ho, J-D.; Keller, JJ; Tsai, C-Y; Liou, S-W; Chang, C-J; Lin, H-C. (2013) Topiramate use and the risk of glaucoma development: A population-based follow-up study. American Journal of Ophthalmology. 155: 336-341.

UCSF/SFVAMC --- PI: S. Batki

Subject #_____-☐☐☐-☐☐ Week 00 Date☐☐/☐☐/☐☐

CAPS

National Center for PTSD

CLINICIAN-ADMINISTERED PTSD SCALE FOR DSM-IV

Name: _____ ID#: _____

Interviewer: _____ Date: _____

Study: _____

Dudley D. Blake, Frank W. Weathers, Linda M. Nagy,
Danny G. Kaloupek, Dennis S. Charney, & Terence M. Keane

National Center for Posttraumatic Stress Disorder

Behavioral Science Division -- Boston VA Medical Center
Neurosciences Division -- West Haven VA Medical Center

Revised July 1998

NOTE-AREAS HIGHLIGHTED IN YELLOW INDICATE INFORMATION TAKEN FROM:

Criterion A. The person has been exposed to a traumatic event in which both of the following were present:

(1) The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others

(2) The person's response involved intense fear, helplessness, or horror. Note: In children, this may be expressed instead by disorganized or agitated behavior (Criterion A-2 not needed for DSM-5)

OR

Criterion A. Criterion A: Exposure to actual or threatened death, serious injury, or sexual violence, in one or more of the following ways:

1. **Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.**
2. **Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains; police officers repeatedly exposed to details of child abuse). Note: This does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work-related.**

I'm going to be asking you about some difficult or stressful things that sometimes happen to people. Some examples of this are being in some type of serious accident; being in a fire, a hurricane, or an earthquake; being mugged or beaten up or attacked with a weapon; or being forced to have sex when you didn't want to. I'll start by asking you to look over a list of experiences like this and check any that apply to you. Then, if any of them do apply to you, I'll ask you to briefly describe what happened and how you felt at the time.

Some of these experiences may be hard to remember or may bring back uncomfortable memories or feelings. People often find that talking about them can be helpful, but it's up to you to decide how much you want to tell me. As we go along, if you find yourself becoming upset, let me know and we can slow down and talk about it. Also, if you have any questions or you don't understand something, please let me know. Do you have any questions before we start?

ADMINISTER CHECKLIST, THEN REVIEW AND INQUIRE UP TO THREE EVENTS. IF MORE THAN THREE EVENTS ENDORSED, DETERMINE WHICH THREE EVENTS TO INQUIRE (E.G., FIRST, WORST, AND MOST RECENT EVENTS; THREE WORST EVENTS; TRAUMA OF INTEREST PLUS TWO OTHER WORST EVENTS, ETC.)

IF NO EVENTS ENDORSED ON CHECKLIST: *(Has there ever been a time when your life was in danger or you were seriously injured or harmed?)*

IF NO: *(What about a time when you were threatened with death or serious injury, even if you weren't actually injured or harmed?)*

IF NO: *(What about witnessing something like this happen to someone else or finding out that it happened to someone close to you?)*

IF NO: *(What would you say are some of the most stressful experiences you have had over your life?)*

EVENT #1

What happened? *(How old were you? What was the date of the event? Who else was involved? How many times did this happen? Life threat? Serious injury?)* ***MUST ASK "TIME SINCE EVENT" [Format Years/Months]*** **How did you respond emotionally?** *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*Describe (e.g., event type, victim, perpetrator, age, frequency):* *A. (1)* *Date of event Month_____ Year_____* *Time since event Years_____ Months_____* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

EVENT #2

What happened? *(How old were you? What was the date of the event? Who else was involved? How many times did this happen? Life threat? Serious injury?)* ***MUST ASK "TIME SINCE EVENT" [Format Years/Months]*** **How did you respond emotionally?** *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*Describe (e.g., event type, victim, perpetrator, age, frequency):* *A. (1)* *Date of event Month_____ Year_____* *Time since event Years_____ Months_____* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

EVENT #3

What happened? *(How old were you? What was the date of the event? Who else was involved? How many times did this happen? Life threat? Serious injury?)* ***MUST ASK "TIME SINCE EVENT" [Format Years/Months]***	*Describe (e.g., event type, victim, perpetrator, age, frequency):*
	A. (1) *Date of event Month_____ Year_____*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event -- how did you respond emotionally?)*	*Time since event Years_____ Months_____* *Life threat? NO YES [self ___ other ___]* *Serious injury? NO YES [self ___ other ___]* *Threat to physical integrity? NO YES [self ___ other ___]* *A. (2)* *Intense fear/help/horror? NO YES [during ___ after ___]* *Criterion A met? NO PROBABLE YES*

For the rest of the interview, I want you to keep (EVENTS) in mind as I ask you some questions about how they may have affected you.

I'm going to ask you about twenty-five questions altogether. Most of them have two parts. First, I'll ask if you've ever had a particular problem, and if so, about how often in the past month. Then I'll ask you how much distress or discomfort that problem may have caused you.

Criterion B. The traumatic event is persistently reexperienced in one (or more) of the following ways:

1. (B-1) Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. **Note:** In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.

Frequency	***Intensity***	
Have you ever had unwanted memories of (EVENT)? What were they like? *(What did you remember?)* [IF NOT CLEAR:] *(Did they ever occur while you were awake, or only in dreams?)* [EXCLUDE IF MEMORIES OCCURRED ONLY DURING DREAMS] **How often have you had these memories in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did these memories cause you? Were you able to put them out of your mind and think about something else?** *(How hard did you have to try?)* **How much did they interfere with your life?** 0 None 1 Mild, minimal distress or disruption of activities 2 Moderate, distress clearly present but still manageable, some disruption of activities 3 Severe, considerable distress, difficulty dismissing memories, marked disruption of activities 4 Extreme, incapacitating distress, cannot dismiss memories, unable to continue activities ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

2. (B-2) Recurrent distressing dreams of the event. **Note:** In children, there may be frightening dreams without recognizable content.

Frequency	***Intensity***	
Have you ever had unpleasant dreams about (EVENT)? Describe a typical dream. *(What happens in them?)* **How often have you had these dreams in the past month? # of times _____** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did these dreams cause you? Did they ever wake you up?** [IF YES:] *(What happened when you woke up? How long did it take you to get back to sleep?)* [LISTEN FOR REPORT OF ANXIOUS AROUSAL, YELLING, ACTING OUT THE NIGHTMARE] *(Did your dreams ever affect anyone else? How so?)* 0 None 1 Mild, minimal distress, may not have awoken 2 Moderate, awoke in distress but readily returned to sleep 3 Severe, considerable distress, difficulty returning to sleep 4 Extreme, incapacitating distress, did not return to sleep ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

3. (B-3) Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). **Note:** In young children, trauma-specific reenactment may occur.

Frequency	***Intensity***	
Have you ever suddenly acted or felt as if (EVENT) were happening again? *(Have you ever had flashbacks about [EVENT]?)* [IF NOT CLEAR:] *(Did this ever occur while you were awake, or only in dreams?)* [EXCLUDE IF OCCURRED ONLY DURING DREAMS] **Tell me more about that. How often has that happened in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much did it seem as if (EVENT) were happening again?** *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No reliving 1 Mild, somewhat more realistic than just thinking about event 2 Moderate, definite but transient dissociative quality, still very aware of surroundings, daydreaming quality 3 Severe, strongly dissociative (reports images, sounds, or smells) but retained some awareness of surroundings 4 Extreme, complete dissociation (flashback), no awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout) ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

4. (B-4) Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

Frequency	***Intensity***	
Have you ever gotten emotionally upset when something reminded you of (EVENT)? *(Has anything ever triggered bad feelings related to [EVENT]?)* **What kinds of reminders made you upset? How often in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did (REMINDERS) cause you? How long did it last? How much did it interfere with your life?** 0 None 1 Mild, minimal distress or disruption of activities 2 Moderate, distress clearly present but still manageable, some disruption of activities 3 Severe, considerable distress, marked disruption of activities 4 Extreme, incapacitating distress, unable to continue activities ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

5. (B-5) Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

Frequency	***Intensity***	
Have you ever had any physical reactions when something reminded you of (EVENT)? *(Did your body ever react in some way when something reminded you of [EVENT]?)* **Can you give me some examples?** *(Did your heart race or did your breathing change? What about sweating or feeling really tense or shaky?)* **What kinds of reminders triggered these reactions? How often in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong were (PHYSICAL REACTIONS)? How long did they last?** *(Did they last even after you were out of the situation?)* 0 No physical reactivity 1 Mild, minimal reactivity 2 Moderate, physical reactivity clearly present, may be sustained if exposure continues 3 Severe, marked physical reactivity, sustained throughout exposure 4 Extreme, dramatic physical reactivity, sustained arousal even after exposure has ended ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

Criterion C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

6. (C-1) Efforts to avoid thoughts, feelings, or conversations associated with the trauma

Frequency	***Intensity***	
Have you ever tried to avoid thoughts or feelings about (EVENT)? *(What kinds of thoughts or feelings did you try to avoid?)* **What about trying to avoid talking with other people about it?** *(Why is that?)* **How often in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much effort did you make to avoid (THOUGHTS/FEELINGS/CONVERSATIONS)?** *(What kinds of things did you do? What about drinking or using medication or street drugs?)* [CONSIDER ALL ATTEMPTS AT AVOIDANCE, INCLUDING DISTRACTION, SUPPRESSION, AND USE OF ALCOHOL/DRUGS] **How much did that interfere with your life?** 0 None 1 Mild, minimal effort, little or no disruption of activities 2 Moderate, some effort, avoidance definitely present, some disruption of activities 3 Severe, considerable effort, marked avoidance, marked disruption of activities, or involvement in certain activities as avoidant strategy 4 Extreme, drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

7. (C-2) Efforts to avoid activities, places, or people that arouse recollections of the trauma

Frequency	***Intensity***	
Have you ever tried to avoid certain activities, places, or people that reminded you of (EVENT)? *(What kinds of things did you avoid? Why is that?)* **How often in the past month?** *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much effort did you make to avoid (ACTIVITIES/PLACES/PEOPLE)?** *(What did you do instead?)* **How much did that interfere with your life?** 0 None 1 Mild, minimal effort, little or no disruption of activities 2 Moderate, some effort, avoidance definitely present, some disruption of activities 3 Severe, considerable effort, marked avoidance, marked disruption of activities or involvement in certain activities as avoidant strategy 4 Extreme, drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify) _____***	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

8. (C-3) Inability to recall an important aspect of the trauma

Frequency	***Intensity***	
Have you had difficulty remembering some important parts of (EVENT)? Tell me more about that. *(Do you feel you should be able to remember these things? Why do you think you can't?)* **In the past month, how much of the important parts of (EVENT) have you had difficulty remembering?** *(What parts do you still remember?)* [If not clear:] (Why do you think you can't? Did you have a head injury during [EVENT]? Were you knocked unconscious? Were you intoxicated from alcohol or drugs?) [Rate 0=Absent if due to head injury or loss of consciousness or intoxication during event] [If still not clear:] (Is this just normal forgetting? Or do you think you may have blocked it out because it would be too painful to remember?) [Rate 0=Absent if due only to normal forgetting] *# of important aspects* _____ 0 None, clear memory 1 Few aspects not remembered (less than 10%) 2 Some aspects not remembered (approx 20-30%) 3 Many aspects not remembered (approx 50-60%) 4 Most or all aspects not remembered (more than 80%) ***Description/Examples***	**How much difficulty did you have recalling important parts of (EVENT)?** *(Were you able to recall more if you tried?)* 0 None 1 Mild, minimal difficulty 2 Moderate, some difficulty, could recall with effort 3 Severe, considerable difficulty, even with effort 4 Extreme, completely unable to recall important aspects of event ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

(DSM-5 D2) Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," "The world is completely dangerous"). (Alternatively, this might be expressed as, e.g., I've lost my soul forever," "My whole nervous system is permanently ruined.")

In the past month, have you had strong negative beliefs about yourself, other people, or the world? **Can you give me some examples?** *(What about believing things like "I am bad," "there is something seriously wrong with me," "no one can be trusted," "the world is completely dangerous"?)* **How strong are these beliefs?** *(How convinced are you that these beliefs are actually true? Can you see other ways of thinking about it?)* Circle: Conviction = *Minimal* *Clearly Present* *Pronounced* *Extreme* **How much of the time in the past month have you felt that way?** *% of time* _____ **Did these beliefs start or get worse after (EVENT)?** *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* ***Key rating dimensions = frequency / intensity of beliefs*** Moderate = some of the time (20-30%) / exaggerated negative expectations clearly present, some difficulty considering more realistic beliefs Severe = much of the time (50-60%) / pronounced exaggerated negative expectations, considerable difficulty considering more realistic beliefs	**0** ***Absent*** **1** ***Mild / subthreshold*** **2** ***Moderate / threshold*** **3** ***Severe / markedly elevated*** **4** ***Extreme / incapacitating***

(DSM-5 D3) Persistent, distorted blame of self or others about the cause or consequences of the traumatic event(s).

In the past month, have you blamed yourself or others for (EVENT) or what happened as a result of it? By others, I don't mean someone who meant to harm you, but someone you think should have known about (EVENT) or been able to stop it. **Tell me more about that.** *(In what sense do you see [YOURSELF OR OTHERS] as responsible?)* [Rate 0=Absent if only blames perpetrator] **How strongly do you blame (YOURSELF OR OTHERS)?** *(How convinced are you that [YOU OR OTHERS] are truly responsible for what happened? Can you see other ways of thinking about it?)* Circle: Conviction = *Minimal* *Clearly Present* *Pronounced* *Extreme* **How much of the time in the past month have you felt that way?** *% of time* _____ ***Key rating dimensions = frequency / intensity of blame*** Moderate = some of the time (20-30%) / distorted blame clearly present, some difficulty considering more realistic beliefs Severe = much of the time (50-60%) / pronounced distorted blame, considerable difficulty considering more realistic beliefs	**0** ***Absent*** **1** ***Mild / subthreshold*** **2** ***Moderate / threshold*** **3** ***Severe / markedly elevated*** **4** ***Extreme / incapacitating***

(DSM-5 D4) Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).

In the past month, have you had any strong negative feelings such as fear, horror, anger, guilt, or shame? **Can you give me some examples?** *(What negative feelings do you experience?)* **How strong are these negative feelings?** **How well are you able to manage them?** Circle: Negative emotions = *Minimal* *Clearly Present* *Pronounced* *Extreme* **How much of the time in the past month have you felt that way?** *% of time* _____ **Did these negative feelings start or get worse after (EVENT)?** *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* ***Key rating dimensions = frequency / intensity of negative emotions*** Moderate = some of the time (20-30%) / negative emotions clearly present, some difficulty managing Severe = much of the time (50-60%) / pronounced negative emotions, considerable difficulty managing	**0** ***Absent*** **1** ***Mild / subthreshold*** **2** ***Moderate / threshold*** **3** ***Severe / markedly elevated*** **4** ***Extreme / incapacitating***

9. (C-4) Markedly diminished interest or participation in significant activities

Frequency	***Intensity***	
Have you been less interested in activities that you used to enjoy? *(What kinds of things have you lost interest in? Are there some things you don't do at all anymore? Why is that?)* [EXCLUDE IF NO OPPORTUNITY, IF PHYSICALLY UNABLE, OR IF DEVELOPMENTALLY APPROPRIATE CHANGE IN PREFERRED ACTIVITIES] **In the past month, how many activities have you been less interested in?** *(What kinds of things do you still enjoy doing?)* **When did you first start to feel that way?** *(After the [EVENT]?)* *% of activities* _____ *(Do you think it's related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* 0 None 1 Few activities (less than 10%) 2 Some activities (approx 20-30%) 3 Many activities (approx 50-60%) 4 Most or all activities (more than 80%) ***Description/Examples***	**How strong was your loss of interest?** *(Would you enjoy [ACTIVITIES] once you got started?)* 0 No loss of interest 1 Mild, slight loss of interest, probably would enjoy after starting activities 2 Moderate, definite loss of interest, but still has some enjoyment of activities 3 Severe, marked loss of interest in activities 4 Extreme, complete loss of interest, no longer participates in any activities ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

10. (C-5) Feeling of detachment or estrangement from others

Frequency

Have you felt distant or cut off from other people? What was that like? How much of the time in the past month have you felt that way? When did you first start to feel that way? *(After the [EVENT]?)*

% *of time* _____

(Do you think it's related to [EVENT]? How so?) Circle:
Trauma-relatedness = *Definite Probable Unlikely*

0 None of the time
1 Very little of the time (less than 10%)
2 Some of the time (approx 20-30%)
3 Much of the time (approx 50-60%)
4 Most or all of the time (more than 80%)

Description/Examples

Intensity

How strong were your feelings of being distant or cut off from others? *(Who do you feel closest to? How many people do you feel comfortable talking with about personal things?)*

0 No feelings of detachment or estrangement
1 Mild, may feel "out of synch" with others
2 Moderate, feelings of detachment clearly present, but still feels some interpersonal connection
3 Severe, marked feelings of detachment or estrangement from most people, may feel close to only one or two people
4 Extreme, feels completely detached or estranged from others, not close with anyone

QV (specify) _____

Trauma-related? *1 definite 2 probable 3 unlikely*

Current _____ *Lifetime* _____

Past month

F _____

I _____

Sx: Y N

11. (C-6) Restricted range of affect (e.g., unable to have loving feelings)

Frequency

Have there been times when you felt emotionally numb or had trouble experiencing feelings like love or happiness? What was that like? *(What feelings did you have trouble experiencing?)* **How much of the time in the past month have you felt that way? When did you first start having trouble experiencing (EMOTIONS)?** *(After the [EVENT]?)*

% *of time* _____

(Do you think it's related to [EVENT]? How so?) Circle:
Trauma-relatedness = *Definite Probable Unlikely*

0 None of the time
1 Very little of the time (less than 10%)
2 Some of the time (approx 20-30%)
3 Much of the time (approx 50-60%)
4 Most or all of the time (more than 80%)

Description/Examples

Intensity

How much trouble did you have experiencing (EMOTIONS)? *(What kinds of feelings were you still able to experience?)* [INCLUDE OBSERVATIONS OF RANGE OF AFFECT DURING INTERVIEW]

0 No reduction of emotional experience
1 Mild, slight reduction of emotional experience
2 Moderate, definite reduction of emotional experience, but still able to experience most emotions
3 Severe, marked reduction of experience of at least two primary emotions (e.g., love, happiness)
4 Extreme, completely lacking emotional experience

QV (specify) _____

Trauma-related? *1 definite 2 probable 3 unlikely*

Current _____ *Lifetime* _____

Past month

F _____

I _____

Sx: Y N

12. (C-7) Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

Frequency	***Intensity***	
Have there been times when you felt there is no need to plan for the future, that somehow your future will be cut short? Why is that? [RULE OUT REALISTIC RISKS SUCH AS LIFE-THREATENING MEDICAL CONDITIONS] **How much of the time in the past month have you felt that way? When did you first start to feel that way?** *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How strong was this feeling that your future will be cut short?** *(How long do you think you will live? How convinced are you that you will die prematurely?)* 0 No sense of a foreshortened future 1 Mild, slight sense of a foreshortened future 2 Moderate, sense of a foreshortened future definitely present, but no specific prediction about longevity 3 Severe, marked sense of a foreshortened future, may make specific prediction about longevity 4 Extreme, overwhelming sense of a foreshortened future, completely convinced of premature death ***QV (specify) _____*** ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

Criterion D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

13. (D-1) Difficulty falling or staying asleep

Frequency	***Intensity***	
Have you had any problems falling or staying asleep? How often in the past month? When did you first start having problems sleeping? *(After the [EVENT]?)* *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite Probable Unlikely* Sleep onset problems? Y N Mid-sleep awakening? Y N Early a.m. awakening? Y N Total # hrs sleep/night _____ Desired # hrs sleep/night _____	**How much of a problem did you have with your sleep?** *(How long did it take you to fall asleep? How often did you wake up in the night? Did you often wake up earlier than you wanted to? How many total hours did you sleep each night?)* 0 No sleep problems 1 Mild, slightly longer latency, or minimal difficulty staying asleep (up to 30 minutes loss of sleep) 2 Moderate, definite sleep disturbance, clearly longer latency, or clear difficulty staying asleep (30-90 minutes loss of sleep) 3 Severe, much longer latency, or marked difficulty staying asleep (90 min to 3 hrs loss of sleep) 4 Extreme, very long latency, or profound difficulty staying asleep (> 3 hrs loss of sleep) ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

14. (D-2) Irritability or outbursts of anger

Frequency	***Intensity***	
Have there been times when you felt especially irritable or showed strong feelings of anger? Can you give me some examples? How often in the past month? When did you first start feeling that way? *(After the [EVENT]?)* *# of times* _____ *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite Probable Unlikely* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was your anger?** *(How did you show it?)* [IF REPORTS SUPPRESSION:] *(How hard was it for you to keep from showing your anger?)* **How long did it take you to calm down? Did your anger cause you any problems?** 0 No irritability or anger 1 Mild, minimal irritability, may raise voice when angry 2 Moderate, definite irritability or attempts to suppress anger, but can recover quickly 3 Severe, marked irritability or marked attempts to suppress anger, may become verbally or physically aggressive when angry 4 Extreme, pervasive anger or drastic attempts to suppress anger, may have episodes of physical violence ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

(DSM-5 E2) Reckless or self-destructive behavior.

In the past month, have there been times when you were taking more risks or doing things that might have caused you harm? **Can you give me some examples?** **How much of a risk do you take?** *(How dangerous are these behaviors? Were you injured or harmed in some way?)* Circle: Risk = *Minimal* *Clearly Present* *Pronounced* *Extreme* **How often have you taken these kinds of risks in the past month?** *# of times* _____ **Did this behavior start or get worse after (EVENT)?** *(Do you think it's related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* ***Key rating dimensions = frequency / degree of risk*** Moderate = at least 2 X month / risk clearly present, may have been harmed Severe = at least 2 X week / pronounced risk, actual harm or high probability of harm	**0** ***Absent*** **1** ***Mild / subthreshold*** **2** ***Moderate / threshold*** **3** ***Severe / markedly elevated*** **4** ***Extreme / incapacitating***

15. (D-3) Difficulty concentrating

Frequency **Have you found it difficult to concentrate on what you were doing or on things going on around you? What was that like? How much of the time in the past month? When did you first start having trouble concentrating?** *(After the [EVENT]?)* *% of time* _____ *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite* *Probable* *Unlikely* ***Description/Examples***	***Intensity*** **How difficult was it for you to concentrate?** [INCLUDE OBSERVATIONS OF CONCENTRATION AND ATTENTION IN INTERVIEW] **How much did that interfere with your life?** 0 No difficulty with concentration 1 Mild, only slight effort needed to concentrate, little or no disruption of activities 2 Moderate, definite loss of concentration but could concentrate with effort, some disruption of activities 3 Severe, marked loss of concentration even with effort, marked disruption of activities 4 Extreme, complete inability to concentrate, unable to engage in activities ***QV (specify)*** _____ ***Trauma-related?*** *1 definite* *2 probable* *3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

16. (D-4) Hypervigilance

Frequency	***Intensity***	
Have you been especially alert or watchful, even when there was no real need to be? *(Have you felt as if you were constantly on guard?)* **Why is that? How much of the time in the past month? When did you first start acting that way?** *(After the [EVENT]?)* *% of time* _____ *(Do you think it's related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite Probable Unlikely* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How hard did you try to be watchful of things going on around you?** [INCLUDE OBSERVATIONS OF HYPERVIGILANCE IN INTERVIEW] **Did your (HYPERVIGILANCE) cause you any problems?** 0 No hypervigilance 1 Mild, minimal hypervigilance, slight heightening of awareness 2 Moderate, hypervigilance clearly present, watchful in public (e.g., chooses safe place to sit in a restaurant or movie theater) 3 Severe, marked hypervigilance, very alert, scans environment for danger, exaggerated concern for safety of self/family/home 4 Extreme, excessive hypervigilance, efforts to ensure safety consume significant time and energy and may involve extensive safety/checking behaviors, marked watchfulness during interview ***QV (specify) _____*** ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

17. (D-5) Exaggerated startle response

Frequency	***Intensity***	
Have you had any strong startle reactions? When did that happen? *(What kinds of things made you startle?)* **How often in the past month? When did you first have these reactions?** *(After the [EVENT]?)* *# of times* _____ *(Do you think they're related to [EVENT]? How so?)* Circle: Trauma-relatedness = *Definite Probable Unlikely* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong were these startle reactions?** *(How strong were they compared to how most people would respond?)* **How long did they last?** 0 No startle reaction 1 Mild, minimal reaction 2 Moderate, definite startle reaction, feels "jumpy" 3 Severe, marked startle reaction, sustained arousal following initial reaction 4 Extreme, excessive startle reaction, overt coping behavior (e.g., combat veteran who "hits the dirt") ***QV (specify) _____*** ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

Criterion E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.

18. Onset of symptoms

[IF NOT ALREADY CLEAR:] **When did you first start having (PTSD SYMPTOMS) you've told me about?** *(How long after the trauma did they start? More than six months?)*	_____ ***total # months delay in onset*** ***With delayed onset (≥ 6 months)? NO YES***

19. Duration of symptoms

[CURRENT] **How long have these (PTSD SYMPTOMS) lasted altogether?**		***Current***
	Duration more than 1 month?	***NO YES***
	Total # months duration	_____
	Acute (< 3 months) or chronic (≥ 3 months)?	***acute chronic***

Criterion F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

20. Subjective distress

[CURRENT] **Overall, how much have you been bothered by these (PTSD SYMPTOMS) you've told me about?** [CONSIDER DISTRESS REPORTED ON EARLIER ITEMS]	0	None	***Past month*** _____
	1	Mild, minimal distress	
	2	Moderate, distress clearly present but still manageable	
	3	Severe, considerable distress	
	4	Extreme, incapacitating distress	

21. Impairment in social functioning

[CURRENT] **Have these (PTSD SYMPTOMS) affected your relationships with other people? How so?** [CONSIDER IMPAIRMENT IN SOCIAL FUNCTIONING REPORTED ON EARLIER ITEMS]	0	No adverse impact	***Past month*** _____
	1	Mild impact, minimal impairment in social functioning	
	2	Moderate impact, definite impairment, but many aspects of social functioning still intact	
	3	Severe impact, marked impairment, few aspects of social functioning still intact	
	4	Extreme impact, little or no social functioning	

22. Impairment in occupational or other important area of functioning

[CURRENT -- IF NOT ALREADY CLEAR] **Are you working now?** IF YES: **Have these (PTSD SYMPTOMS) affected your work or your ability to work? How so?** [CONSIDER REPORTED WORK HISTORY, INCLUDING NUMBER AND DURATION OF JOBS, AS WELL AS THE QUALITY OF WORK RELATIONSHIPS. IF PREMORBID FUNCTIONING IS UNCLEAR, INQUIRE ABOUT WORK EXPERIENCES BEFORE THE TRAUMA. FOR CHILD/ADOLESCENT TRAUMAS, ASSESS PRE-TRAUMA SCHOOL PERFORMANCE AND POSSIBLE PRESENCE OF BEHAVIOR PROBLEMS] IF NO: **Have these (PTSD SYMPTOMS) affected any other important part of your life?** [AS APPROPRIATE, SUGGEST EXAMPLES SUCH AS PARENTING, HOUSEWORK, SCHOOLWORK, VOLUNTEER WORK, ETC.] **How so?**	0 1 2 3 4	No adverse impact Mild impact, minimal impairment in occupational/other important functioning Moderate impact, definite impairment, but many aspects of occupational/other important functioning still intact Severe impact, marked impairment, few aspects of occupational/other important functioning still intact Extreme impact, little or no occupational/other important functioning	***Past month*** ____

Global Ratings

23. Global validity

ESTIMATE THE OVERALL VALIDITY OF RESPONSES. CONSIDER FACTORS SUCH AS COMPLIANCE WITH THE INTERVIEW, MENTAL STATUS (E.G., PROBLEMS WITH CONCENTRATION, COMPREHENSION OF ITEMS, DISSOCIATION), AND EVIDENCE OF EFFORTS TO EXAGGERATE OR MINIMIZE SYMPTOMS.	0 1 2 3 4	Excellent, no reason to suspect invalid responses Good, factors present that may adversely affect validity Fair, factors present that definitely reduce validity Poor, substantially reduced validity Invalid responses, severely impaired mental status or possible deliberate “faking bad” or “faking good”	***Past month*** ____

24. Global severity

ESTIMATE THE OVERALL SEVERITY OF PTSD SYMPTOMS. CONSIDER DEGREE OF SUBJECTIVE DISTRESS, DEGREE OF FUNCTIONAL IMPAIRMENT, OBSERVATIONS OF BEHAVIORS IN INTERVIEW, AND JUDGMENT REGARDING REPORTING STYLE.	0 1 2 3 4	No clinically significant symptoms, no distress and no functional impairment Mild, minimal distress or functional impairment Moderate, definite distress or functional impairment but functions satisfactorily with effort Severe, considerable distress or functional impairment, limited functioning even with effort Extreme, marked distress or marked impairment in two or more major areas of functioning	***Past month*** ____

25. Global improvement

RATE TOTAL OVERALL IMPROVEMENT PRESENT SINCE THE INITIAL RATING. IF NO EARLIER RATING, ASK HOW THE SYMPTOMS ENDORSED HAVE CHANGED OVER THE PAST 6 MONTHS. RATE THE DEGREE OF CHANGE, WHETHER OR NOT, IN YOUR JUDGMENT, IT IS DUE TO TREATMENT.	0 Asymptomatic 1 Considerable improvement 2 Moderate improvement 3 Slight improvement 4 No improvement 5 Insufficient information	***Past month*** _____

Current PTSD Symptoms

Criterion A met (traumatic event)? *NO* *YES*

_____ *# Criterion B sx (≥ 1)?* *NO* *YES*

_____ *# Criterion C sx (≥ 3)?* *NO* *YES*

_____ *# Criterion D sx (≥ 2)?* *NO* *YES*

Criterion E met (duration ≥ 1 month)? *NO* *YES*

Criterion F met (distress/impairment)? *NO* *YES*

_____

CURRENT PTSD (Criteria A-F met)? *NO* *YES*

IF CURRENT PTSD CRITERIA ARE MET, CONTINUE TO ASSOCIATED FEATURES.

Associated Features

26. Guilt over acts of commission or omission

Frequency **Have you felt guilty about anything you did or didn't do during (EVENT)? Tell me more about that.** *(What do you feel guilty about?)* **How much of the time have you felt that way in the past month?** 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	***Intensity*** **How strong were these feelings of guilt? How much distress or discomfort did they cause?** 0 No feelings of guilt 1 Mild, slight feelings of guilt 2 Moderate, guilt feelings definitely present, some distress but still manageable 3 Severe, marked feelings of guilt, considerable distress 4 Extreme, pervasive feelings of guilt, self-condemnation regarding behavior, incapacitating distress ***QV (specify)*** _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

27. Survivor guilt [APPLICABLE ONLY IF MULTIPLE VICTIMS]

Frequency	***Intensity***	
Have you felt guilty about surviving (EVENT) when others did not? Tell me more about that. *(What do you feel guilty about?)* **How much of the time have you felt that way in the past month?** 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx 20-30%) 3 Much of the time (approx 50-60%) 4 Most or all of the time (more than 80%) 8 N/A ***Description/Examples***	**How strong were these feelings of guilt? How much distress or discomfort did they cause?** 0 No feelings of guilt 1 Mild, slight feelings of guilt 2 Moderate, guilt feelings definitely present, some distress but still manageable 3 Severe, marked feelings of guilt, considerable distress 4 Extreme, pervasive feelings of guilt, self-condemnation regarding survival, incapacitating distress ***QV (specify) _____***	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

28. A reduction in awareness of his or her surroundings (e.g., **"**being in a daze")

Frequency	***Intensity***	
Have there been times when you felt out of touch with things going on around you, like you were in a daze? What was that like? [DISTINGUISH FROM FLASHBACK EPISODES] **How often has that happened in the past month?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was this feeling of being out of touch or in a daze?** *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No reduction in awareness 1 Mild, slight reduction in awareness 2 Moderate, definite but transient reduction in awareness, may report feeling "spacy" 3 Severe, marked reduction in awareness, may persist for several hours 4 Extreme, complete loss of awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout) ***QV (specify) _____*** ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current _____ Lifetime _____*	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

29. Derealization

Frequency	***Intensity***	
Have there been times when things going on around you seemed unreal or very strange and unfamiliar? [IF NO:] *(What about times when people you knew suddenly seemed unfamiliar?)* **What was that like? How often has that happened in the past month?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* *# of times _____* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was (DEREALIZATION)? How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No derealization 1 Mild, slight derealization 2 Moderate, definite but transient derealization 3 Severe, considerable derealization, marked confusion about what is real, may persist for several hours 4 Extreme, profound derealization, dramatic loss of sense of reality or familiarity ***QV (specify) _____*** ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current _____ Lifetime _____*	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

30. Depersonalization

Frequency	***Intensity***	
Have there been times when you felt as if you were outside of your body, watching yourself as if you were another person? [IF NO:] *(What about times when your body felt strange or unfamiliar to you, as if it had changed in some way?)* **What was that like? How often has that happened in the past month?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)* *# of times* _____ 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How strong was (DEPERSONALIZATION)? How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No depersonalization 1 Mild, slight depersonalization 2 Moderate, definite but transient depersonalization 3 Severe, considerable depersonalization, marked sense of detachment from self, may persist for several hours 4 Extreme, profound depersonalization, dramatic sense of detachment from self ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Past month*** ***F*** _____ ***I*** _____ ***Sx: Y N***

CAPS SUMMARY SHEET (DSM-IV)

Name:_____ ID#:_____ Interviewer:_____ Study:_____ Date:_____

A. Traumatic event:

B. Reexperiencing symptoms	*PAST MONTH*		
	Freq	*Int*	*F+I*
(1) intrusive recollections			
(2) distressing dreams			
(3) acting or feeling as if event were recurring			
(4) psychological distress at exposure to cues			
(5) physiological reactivity on exposure to cues			
B subtotals			
Number of Criterion B symptoms (need 1)			

C. Avoidance and numbing symptoms	*PAST MONTH*		
	Freq	*Int*	*F+I*
(6) avoidance of thoughts or feelings			
(7) avoidance of activities, places, or people			
(8) inability to recall important aspect of trauma			
(9) diminished interest in activities			
(10) detachment or estrangement			
(11) restricted range of affect			
(12) sense of a foreshortened future			
C subtotals			
Number of Criterion C symptoms (need 3)			

D. Hyperarousal symptoms	*PAST MONTH*		
	Freq	*Int*	*F+I*
(13) difficulty falling or staying asleep			
(14) irritability or outbursts of anger			
(15) difficulty concentrating			
(16) hypervigilance			
(17) exaggerated startle response			
D subtotals			
Number of Criterion D symptoms (need 2)			

Total Freq, Int, and Severity (F+I)	*PAST MONTH*		
	Freq	*Int*	*F+I*
Sum of subtotals (B+C+D)			

E. Duration of disturbance	*CURRENT*
(19) duration of disturbance at least one month	*NO YES*

F. Significant distress or impairment in functioning	*PAST MONTH*
(20) subjective distress	
(21) impairment in social functioning	
(22) impairment in occupational functioning	
AT LEAST ONE ≥ 2?	*NO YES*

PTSD diagnosis	*CURRENT*
PTSD PRESENT -- ALL CRITERIA (A-F) MET?	*NO YES*
Specify: (18) with delayed onset (≥ 6 months delay)	*NO YES*
(19) acute (< 3 months) or chronic (≥ 3 months)	*acute chronic*

Global ratings	*PAST MONTH*
(23) global validity	
(24) global severity	
(25) global improvement	

Associated features	*PAST MONTH*		
	Freq	*Int*	*F+I*
(26) guilt over acts of commission or omission			
(27) survivor guilt			
(28) reduction in awareness of surroundings			
(29) derealization			
(30) depersonalization			

PCL-C

INSTRUCTIONS: Below is a list of problems and complaints that people sometimes have in response to stressful life experiences. Please read each one carefully, then fill in the circle to the right to indicate how much you have been bothered by that problem in the past week. Make sure to base your answers on problems that started or got worse after the event.

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Repeated, disturbing *memories, thoughts* or *images* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
2. Repeated, disturbing *dreams* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
3. Suddenly *acting* or *feeling* as if a stressful experience *were happening again* (as if you were reliving it)?	⬭	⬭	⬭	⬭	⬭
4. Feeling *very upset* when *something reminded you* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
5. Having *physical reactions* (e.g., heart pounding, trouble breathing, sweating) when *something reminded you* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
6. Avoiding *thinking about* or *talking about* a stressful experience from the past or avoiding *having feelings* related to it?	⬭	⬭	⬭	⬭	⬭
7. Avoiding *activities* or *situations* because *they reminded you* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
8. Trouble *remembering important parts* of a stressful experience from the past?	⬭	⬭	⬭	⬭	⬭
9. *Loss of interest* in activities that you used to enjoy?	⬭	⬭	⬭	⬭	⬭
10. Feeling *distant* or *cut off* from other people?	⬭	⬭	⬭	⬭	⬭
11. Feeling *emotionally numb* or being unable to have loving feelings for those close to you?	⬭	⬭	⬭	⬭	⬭
12. Feeling as if your future will somehow be *cut short*?	⬭	⬭	⬭	⬭	⬭
13. Trouble *falling* or *staying asleep*?	⬭	⬭	⬭	⬭	⬭
14. Feeling *irritable* or having *angry outbursts*?	⬭	⬭	⬭	⬭	⬭
15. Having difficulty *concentrating*?	⬭	⬭	⬭	⬭	⬭
16. Being *"super-alert"* or watchful or on guard?	⬭	⬭	⬭	⬭	⬭
17. Feeling *jumpy* or easily startled?	⬭	⬭	⬭	⬭	⬭

Date ☐☐ / ☐☐ / ☐☐ ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

ID ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

	Not at all	A little bit	Moderately	Quite a bit	Extremely
18. Having strong negative beliefs about yourself, other people, or the world *(for example, having thoughts such as: I am bad, there is something seriously wrong with me, no one can be trusted, the world is completely dangerous)*?	⬭	⬭	⬭	⬭	⬭
19. Blaming yourself or someone else (who didn't directly cause the event or actually harm you) for the stressful experience or what happened after it?	⬭	⬭	⬭	⬭	⬭
20. Having strong negative feelings such as fear, horror, anger, guilt, or shame?	⬭	⬭	⬭	⬭	⬭
21. Taking too many risks or doing things that could cause you harm?	⬭	⬭	⬭	⬭	⬭

Items 1-17: PCL-C for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD
Items 18-20: PCL-5 for DSM-5 (5/15/2013) Weathers, Litz, Keane, Palmieri, Marx, & Schnurr -- National Center for PTSD

Date

		/		/			ID

UCSF/SFVAMC --- PI: S. Batki

Subject # _____-☐☐☐-☐☐ Week # 00 Date ☐☐/☐☐/☐☐

SCID-I/P, SUDs Section

Structured Clinical Interview for DSM-IV

	CURRENT Abuse [a] Dependence [b] Lifetime alcohol dependence [a] Current Abuse: Meets diagnostic criteria within the last year. [b] Current Dependence: Has met 3 of 7 required symptoms at some point within the last year.	Age of Onset (For Current Abuse and Dependence, or lifetime Alcohol Dependence)	COMMENTS
Alcohol Abuse	● Yes ● No		
Alcohol Dependence	● Yes ● No		
Lifetime alcohol dependence	● Yes ● No	_____	
Cannabis Abuse	● Yes ● No		
Cannabis Dependence	● Yes ● No		
Cocaine Abuse	● Yes ● No		
Cocaine Dependence	● Yes ● No		
Sedative Abuse	● Yes ● No		
Sedative Dependence	● Yes ● No		
Stimulant Abuse	● Yes ● No		
Stimulant Dependance	● Yes ● No		
Opioid Abuse	● Yes ● No		
Opioid Dependence	● Yes ● No		

Source Reference: First, Michael B., Spitzer, Robert L, Gibbon Miriam, and Williams, Janet B.W.: Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P) New York: Biometrics Research, New York State Psychiatric Institute, November 2002. **Reference:** Segal, D.L. Hersen, M., Van Hasselt, V.B. (1994). Reliability of the Structured Clinical Interview for DSM-III-R: an evaluative review. Compr Psychiatry 35: 316-327.	**Obtained from**: SUNY Upstate Medical University Version 2 ~ 10/16/09 R:\Batki Addiction Research\Measures and Manuals\TOP ALC PTSD MEASURES\Measures\SCID-IP, SUDs Section\Measures

SCID-I (for DSM-IV-TR) **SUBSTANCE USE SCREENING QUESTIONS**
ALCOHOL USE

IN GENERAL:
What are your drinking habits like? (How much do you drink?) (Has there ever been a time when you had five or more drinks on one occasion?)

When in your life were you drinking the most? (How long did that period last?)

RECORD DATE OF HEAVIEST USE AND DESCRIBE PATTERN:

_____

During that time how often were you drinking?

What were you drinking? *How much?*

During that time did your drinking cause problems for you?

Did anyone object to your drinking?

IN THE LAST YEAR…What have your drinking habits been like? How much have you been drinking? What have you been drinking? *Has there ever been a time when you had five or more drinks on one occasion in the last year?)*

In the last year… *did your drinking cause problems for you?*
did anyone object to your drinking?

GUIDELINES FOR ADMINISTRATION OF ALCOHOL USE DISORDERS SECTION:

- If subject reports at least 1 incident of 5 or more drinks, acknowledges ever having had a problem relating to drinking, or admits that others objected to drinking, then administer Alcohol Use Disorder section. Ask about Alcohol Abuse section first unless Alcohol Dependence (AD) seems likely. In this case, ask about AD first.

[1] TOLERANCE ➢ OVER THE PAST YEAR did you find that you needed to drink a lot more in order to get the feeling you wanted than you did when you first started drinking? *(How much do you have to drink now to "start to feel a buzz")* IF YES: How much more? IF NO: What about finding that when you drank the same amount, it had much less effect than before? *(How much do you have to drink now to "start to feel a buzz")*	Amount at start of drinking career: _____ Maximum amount in last year: _____ Current amount: _____	WHEN YOU WERE DRINKING THE MOST… Amount at start of drinking career: _____ Maximum amount when you were drinking the most: _____
(1) tolerance, as defined by either of the following: (a) a need for markedly increased amounts of alcohol to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of alcohol	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

[2] (WITHDRAWAL) IN THE PAST YEAR … did you ever have any withdrawal symptoms when you cut down or stopped drinking like… …sweating or racing heart? …hand shakes? …trouble sleeping? …feeling nauseated or vomiting? …feeling agitated? …or feeling anxious? (How about having a seizure or seeing, feeling, or hearing things that weren't really there?) *(Any detox admissions?)* **IF NO:** In the past year, did you ever start the day with a drink, or did you often drink or take some other drug or medication to keep yourself from getting the shakes or becoming sick?		WHEN YOU WERE DRINKING THE MOST… WHEN YOU WERE DRINKING THE MOST…
(2) withdrawal, as manifested by either (a) or (b): (a) at least 2 of the following: □ autonomic hyperactivity (e.g., sweating or pulse rate greater than 100) □ increased hand tremor □ insomnia □ nausea or vomiting □ psychomotor agitation □ anxiety □ grand mal seizures □ transient visual, tactile, or auditory hallucinations or illusions (b) alcohol (or a substance from the sedative/hypnotic/anxiolytic class) taken to relieve or avoid withdrawal symptoms.	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

[3] I'd now like to ask you some more questions about *(a time in the last year when drinking the most*). IN THE PAST YEAR… ➢ Did you often find that when you started drinking you ended up drinking much more than you were planning to? *(Drinking more than you wanted to?)* **If NO**: What about drinking for a much longer period of time than		WHEN YOU WERE DRINKING THE MOST…
NOTE: Criteria for dependence are not in DSM-IV-TR order. (3) alcohol is often taken in larger amounts OR over a longer period than was intended	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?
[4] ➢ IN THE PAST YEAR …did you try to cut down or stop drinking alcohol? *(Even a little bit?)* If YES: Did you ever actually stop drinking altogether? *(Do you worry about "should you"?)* (How many times did you try to cut down or stop altogether?) *(Did you ever try to?)* *(Tell me about those times.)* **If NO**: Did you want to stop or cut down? (Is this something you kept		WHEN YOU WERE DRINKING THE MOST…
(4) there is a persistent desire OR unsuccessful efforts to cut down or control alcohol use	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

[5] ➢ OVER THE PAST YEAR … did you spend a lot of time drinking, being high, or hung over? *(Is alcohol still in your system?)* *(What is your normal schedule?)* *(When do you start feeling 100%?)*		WHEN YOU WERE DRINKING THE MOST…
(5) a great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?
[6] ➢IN THE PAST YEAR …did you have times when you would drink so often that you started to drink instead of working or spending time at hobbies or with your family or friends, or engaging in other important activities, such as sports, gardening, or playing music? *(Has drinking affected other responsibilities like laundry, grocery shopping, or cleaning your house?)* *(What about commitments to friends or family?)* *(What activities have you enjoyed doing in the past?)* *(Do you do them now? Why*		WHEN YOU WERE DRINKING THE MOST…
(6) important social, occupational, or recreational activities given up or reduced because of alcohol use	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

[7] ➢ IF NOT ALREADY KNOWN: OVER THE PAST YEAR … did your drinking cause any psychological problems, like making you depressed or anxious, making it difficult to sleep, or causing "blackouts"? *(Were you more depressed/anxious than usual?)* *(Did drinking make it any more difficult to for you to sleep?)* *(Did you have times when you were drinking and couldn't remember how you wound up in a situation where you didn't know how you got there?)* *(Have you been hospitalized after drinking?)* IF NOT ALREADY KNOWN: OVER THE PAST YEAR …did your drinking cause any significant physical problems or make a physical problem worse? *(Did your doctor tell you your blood pressure/ulcers/heart burn would get worse if you continued to drink?)* *(But you continued to drink throughout that time?)* *(And it was hard for you to stop?)* IF YES TO EITHER OF ABOVE:		WHEN YOU WERE DRINKING THE MOST… WHEN YOU WERE DRINKING THE MOST…
(7) alcohol use is continued despite knowledge of having had a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol (e.g., continued drinking despite recognition that an ulcer was made worse by alcohol consumption)	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

[8] ➢ OVER THE PAST YEAR … have you had a strong desire or urge to use alcohol? *(Have you spent a lot of time thinking about drinking or about how good a drink would make you feel?*		WHEN YOU WERE DRINKING THE MOST…
(5) craving or strong desire, urge to use alcohol	**CURRENT** 3 2 1 ?	**LIFETIME** 3 2 1 ?

ALCOHOL DEPENDENCE CRITERIA *A maladaptive pattern of alcohol use, leading to clinically significant impairment or distress, as manifested by three (or more) of the previous questions* ***(not including item 8)*** *occurring at any time in the same 12-month period:*	**CURRENT (at least 3 of 7 coded 3 in the past year, excluding item 8)** 3 2 1 ?	**LIFETIME (at lease 3 of 7 coded 3 in 12 months in lifetime)** 3 2 1 ?

CURRENT ALCOHOL DEPENDENCE DIAGNOSIS (3 of 7 items met within the last year, excluding item 8) **LIFETIME ALCOHOL DEPENDENCE?**

☐**YES** ☐ **NO**

How old were you when you had (LIST OF DEPENDENCE SX CODED "3"?)

☐ **AGE AT ONSET OF ALCOHOL DEPENDENCE:**

– GO ON -EVALUATE ALCOHOL ABUSE EVEN IF POSITIVE FOR ALCOHOL DEPENDENCE

[1] OVER THE LAST YEAR**:** … did you miss work or school because you were intoxicated, high, or very hung over? (How often? What about doing a bad job at work or failing courses at school because of your drinking?) *(What about appointments with your therapist or doctor?)* **IF NO**: What about not keeping your house clean or not taking proper care of your children because of your drinking? (How often?) *(What about visitation, job interviews, taking your medication as prescribed, money management, self-care or signing up for classes)* **IF YES TO EITHER OF ABOVE**: How often? (Over what period of time?)	
(1) recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to alcohol use; alcohol-related absences; suspensions, or expulsions from school; neglect of children or household)	**CURRENT** **(Last Year)** 3 2 1 ?
[2] OVER THE LAST YEAR …did you ever drink in situations in which it might have been dangerous to drink at all? (Did you ever drive while you were really too drunk to drive?) *(**At least two:** driving, burning yourself, physical situations in bars, wandering around in the cold?)* **IF YES AND UNKNOWN**: How many times? (When?)	
(2) recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by alcohol use)	**CURRENT** **(Last Year)** 3 2 1 ?

[3] OVER THE LAST YEAR …did your drinking get you into trouble with the law? **IF YES AND UNKNOWN**: How often? (Over what period of time?) *(How many times have you been arrested?)*	
(3) recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct)	**CURRENT (Last Year)** 3 2 1 ?

[4] ➢ IF NOT ALREADY KNOWN: OVER THE LAST YEAR, did your drinking cause problems with other people, such as with family members, friends, *(case manager, therapist, doctor),* or people at work? (Did you get into physical fights when you were drinking? What about having bad arguments about your drinking?) *(Has anyone in your life made comments about the amount you drink or how you act when you drink?)* **IF YES**: Did you keep on drinking anyway? (Over what period of time?)	
(4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol (e.g., arguments with spouse about consequences of intoxication, physical fights)	**CURRENT (Last Year)** 3 2 1 ?

ALCOHOL ABUSE CRITERIA	**At least one item is coded 3**
A. A maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by1 (or more) of the following occurring within a 12-month period:	1 3

CURRENT ALCOHOL ABUSE DIAGNOSIS (criteria met with the last year):

☐ **YES** (At least one item is coded "3.")

How old were you when you had (LIST OF ABUSE SX CODED "3"?)

☐ **AGE AT ONSET OF ALCOHOL ABUSE:**

SCID-I (for DSM-IV-TR) Non-Alcohol Use Disorders (NOV 2002) Lifetime Dependence and Abuse

Now I am going to ask you about your use of drugs or medicines.

REFERRING TO LIST ON NEXT PAGE, DETERMINE LEVEL OF DRUG USE USING GUIDELINES BELOW.

GUIDELINES FOR RATING LEVEL OF DRUG USE:

FOR EACH DRUG GROUP EVER USED: Either (1) or (2):

→ **IF STREET DRUG**: When were you using the most?

(Has there ever been a time when you used it at least ten times in a one-month period of time?)

(1) has ever taken street drug more than 10 times in a one-month period.

→ IF PRESCRIBED: Did you ever get hooked (become dependent) on (PRESCRIBED DRUG) or take much more of it than was prescribed?

(2) reports becoming dependent on a prescribed drug OR using much more of it than was prescribed.

→ **IF DRUG GROUP NEVER USED OR USED ONLY ONCE, OR IF PRESCRIBED DRUG USED AS DIRECTED, CIRCLE "1" FOR DRUG GROUP ON PAGE 10.**

→ **IF DRUG GROUP USED AT LEAST TWICE, BUT LESS THAN LEVEL INDICATED ON (1), CODE "2" FOR DRUG GROUP ON PAGE 10.**

→ **IF DRUG GROUP USED AT LEVEL INDICATED IN ITEM (1) OR IF POSSIBLE DEPENDENT ON PRESCRIBED DRUG (ITEM (2) IS TRUE), CODE "3" ON PAGE 10.**

PROMPTS FOR SECTION BELOW:

FOR EACH STREET DRUG: Did you use ___ in the last year? When were you using the most (in the last year)? (*Assess how much person was using.)* Has there ever been a time when you used it at least ten times in a one-month period of time (in the last year?)

IF PRESCRIBED: Did you ever get hooked (become dependent) on (PRESCRIBED DRUG) or take much more of it than was prescribed?

ASSESS PATTERN OF USE OVER LAST YEAR

CIRCLE THE NAME OF EACH DRUG EVER USED (OR WRITE IN NAME IF "OTHER")	- RECORD PERIOD OF HEAVIEST USE IN LAST YEAR (AGE OR DATE, AND DURATION) AND DESCRIBE PATTERN OF USE.	INDICATE LEVEL OF USE OVER LAST YEAR (USE GUIDELINES, P.9) - If never used or used once, or used as prescribed: Code "1." - If used 2-10 times in 1-month time period: Code "2." - If used > 10 times in 1-month period or possibly dependent on prescribed drug: Code "3."
Sedatives-hypnotics-anxiolytics: Quaalude, Seconal, Valium, Xanax, Librium, barbiturates, Miltown, Ativan, Dalmane, Halcion, Restoril, or other: _____		? 1 2 3
Cannabis: marijuana, hashish, THC, or other _____		? 1 2 3
Stimulants: amphetamine, "speed", crystal meth, dexadrine, Ritalin, "ice", or other: _____		? 1 2 3
Opioids: heroin, morphine, opium, Methadone, Darvon, codeine, Percodan, Demerol, Dilaudid, unspecified or other: _____		? 1 2 3
Cocaine: intranasal, IV, freebase, crack, "speedball," unspecified, or other: _____		? 1 2 3

SCID-I (for DSM-IV-TR) Non-Alcohol Dependence (NOV 2002): Cannabis, Sedatives, Stimulants, Cocaine, & Opioids

[1] IN THE PAST YEAR… did you find that you needed to use a lot more (DRUG) in order to get the feeling you wanted than you did when you first started using it? **IF YES**: How much more? **IF NO**: What about finding that when you used the same amount, it had much less effect than before?	**Cannabis:** **Cocaine:** **Sedatives:** **Stimulants**: **Opioids:**
(1) tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of substance	**CURRENT (last year)** **Cannabis** **Sed/hyp/anx** **Stim** **Cocaine** **Opioids** 3 3 3 3 3 2 2 2 2 2 1 1 1 1 1 ? ? ? ? ?

[2]

NOTE: The following item may not apply to cannabis and hallucinogens/PCP.

- IN THE PAST YEAR

…did you ever have withdrawal symptoms, that is, felt sick when you cut down or stopped using (DRUG)?

IF YES: What symptoms did you have? REFER TO LIST OF WITHDRAWAL SYMPTOMS (below)

IF NO: After not using (DRUG) for a few hours or more, did you often use it to keep yourself from getting sick with (WITHDRAWAL SX)?

IF NO: What about using (DRUG IN SAME GROUP) when you were feeling sick with (WITHDRAWAL SXS) so that you would feel better?

(*Nicotine specific - Smoking first thing in the morning or after being in a situation where use is restricted (e.g., at work or on an airplane).*

Cannabis: **Cocaine:**

Sedatives: **Opioids:**

Stimulants:

(2) Withdrawal, as manifested by either of the following:

(a) the characteristic withdrawal syndrome for the substance

(b) the same (or a closely) related substance is taken to relieve or avoid withdrawal symptoms

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

LIST OF WITHDRAWAL SYMPTOMS (listed in SCID - from DSM-IV criteria) **NOTE**: Withdrawal symptoms may occur following the cessation of prolonged moderate or heavy use of a psychoactive substance or a reduction in the amount used.

CANNABIS

Three or more of the following must develop within approximately 1 week following the cessation of cannabis use that has been heavy and prolonged (usually daily or almost daily use over a period of at least a few months).
(1) Irritability, anger, or aggression
(2) Nervousness or anxiety
(3) Sleep difficulty (e.g., insomnia, disturbing dreams).
(4) Decreased appetite or weight loss.
(5) restlessness
(6) Depressed mood
(7) At least one of the following physical symptoms causing sig. discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache

STIMULANTS/COCAINE

Dysphoric Mood AND two (or more) of the following physiological changes, developing within a few hours to several days after cessation (or reduction of substance use which has been heavy and prolonged):
(1) fatigue
(2) vivid, unpleasant dreams
(3) insomnia and hypersomnia
(4) increased appetite
(5) psychomotor retardation or agitation

OPIOIDS

Three (or more) of the following, developing within minutes to several days after cessation (or reduction) of opioid use which has been heavy and prolonged (several weeks or longer) or after administration of an opioid antagonist (after a period of opioid use):
(1) dysphoric mood
(2) nausea or vomiting
(3) muscle aches
(4) lacrimation or rhinorrhea
(5) papillary dilation, piloerection, or sweating
(6) diarrhea
(7) yawning
(8)fever
(9)insomnia

SEDATIVES, HYPNOTICS, AND ANXIOLYTICS

Two (or more) of the following, developing within several hours to a few days after cessation (or reduction) of sedative, hypnotic, or anxiolytic use, which has been heavy and prolonged:
(1) autonomic hyperactivity (e.g., sweating or pulse rate greater than 100)
(2) increased hand tremor
(3) insomnia
(4) nausea or vomiting
(5) transient visual, tactile, or auditory hallucinations or illusions
(6) psychomotor agitation
(7) anxiety
(8) grand mal seizures

[3]

Now I am going to ask you some specific questions about your use of (DRUGS).

For (DRUG), DURING THE PAST YEAR

…did you often find that when you started using (DRUG), you ended up using much more of it than you were planning to?

If NO: What about using it over a much longer period of time than you were planning to?

Cannabis: **Cocaine:**

Sedatives: **Opioids:**

Stimulants:

[3]
NOTE: Criteria for dependence are in a different order than in DSM-IV-TR.

(3) the substance is often taken in larger amounts OR over a longer period than was intended

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[4]

IN THE PAST YEAR

…did you try to cut down or stop using (DRUG) ?

If YES: Did you ever actually stop using DRUG altogether?

(How many times did you try to cut down or stop altogether?)

If UNCLEAR: Did you want to stop or cut down?
If YES: Is this something you kept worrying about?

Cannabis: **Cocaine:**

Sedatives: **Opioids:**

Stimulants:

[4] there is a persistent desire OR unsuccessful efforts to cut down or control substance use

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[5]

IN THE PAST YEAR

…did you spend a lot of time using (DRUG) or doing whatever you had to do to get it? Did it take you a long time to get back to normal? (How much time? As long as several hours?)

Cannabis: **Cocaine:**

Sedatives: **Opioids:**

Stimulants:

[5] a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[6]

IN THE PAST YEAR…

did you often have times when you would use (DRUG) so often that you used (DRUG) instead of working or spending time on hobbies or with your family or friends or engaging in other activities, such as sports, gardening, or playing music?

Cannabis: **Cocaine:**

Sedatives: **Opioids:**

Stimulants:

[6] important social, occupational, or recreational activities given up or reduced because of substance use

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[7]

- IF NOT ALREADY KNOWN:

IN THE PAST YEAR did (DRUG) cause any psychological problems, like making you depressed, agitated, or paranoid?

IF NOT ALREADY KNOWN:
IN THE PAST YEAR …did (DRUG) cause any significant physical problems or make a physical problem worse?

If YES TO EITHER OF ABOVE: Did you keep on using (DRUG) anyway?

Cannabis:

Cocaine:

Sedatives:

Opioids:

Stimulants:

[7] the substance use is continued despite knowledge of having had a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., recurrent cocaine use despite recognition of cocaine-related depression)

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[8] ➢ OVER THE PAST YEAR … have you had a strong desire or urge to use ….? *(Have you spent a lot of time thinking about using … or about how good using … would make you feel?*	**Cannabis:** **Cocaine:** **Sedatives:** **Opioids:** **Stimulants**:

(8) craving or strong desire, urge to use…	**CURRENT (last year)**				
	Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
	3	3	3	3	3
	2	2	2	2	2
	1	1	1	1	1
	?	?	?	?	?

CURRENT SUBSTANCE DEPENDENCE DIAGNOSIS (3 of 7 items met within the last year, excluding item 8)?

Cannabis	☐ Y	☐ N
Sed/hyp/anx	☐ Y	☐ N
Stim	☐ Y	☐ N
Cocaine	☐ Y	☐ N
Opioids	☐ Y	☐ N

– **GO ON -EVALUATE SUBSTANCE ABUSE EVEN IF POSITIVE FOR SUBSTANCE DEPENDENCE**

[1]

NOTE: For each drug class coded "2" (i.e., drugs used at a level of less than 10 times in any one month).

Now I'd like to ask you a few more questions about your use of (DRUG).

For (DRUG), IN THE PAST YEAR).

- Did you miss work or school because you were intoxicated, high, or very hung over? (How often? What about doing a bad job at work or failing courses at school because of your [DRUG] use?

IF NO: What about not keeping your house clean or not taking proper care of your children because of your (DRUG) USE?

IF YES TO EITHER OF ABOVE:
How often? (Over what period of time?)

Cannabis:

Cocaine:

Sedatives:

Opioids:

Stimulants:

SUBSTANCE ABUSE CRITERIA

(1) *A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following occurring with a 12-month period:*

*R*ecurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)

CURRENT (last year)

Cannabis	Sed/hyp/anx	Stim	Cocaine	Opioids
3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
?	?	?	?	?

[2] IN THE PAST YEAR …did you use (DRUG) in a situation in which it might have been dangerous to be using (DRUG) at all? (Did you ever drive while you were really too high to drive?) **IF YES AND UNKNOWN**: How often? (Over what period of time?)	**Cannabis:** **Cocaine:** **Sedatives:** **Opioids:** **Stimulants**:
(2) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)	**CURRENT (last year)** Cannabis Sed/hyp/anx Stim Cocaine Opioids 3 3 3 3 3 2 2 2 2 2 1 1 1 1 1 ? ? ? ? ?
[3] IN THE PAST YEAR …did your use of (DRUG) get you into trouble with the law? **IF YES AND UNKNOWN**: How often? (Over what period of time?)	**Cannabis:** **Cocaine:** **Sedatives:** **Opioids:** **Stimulants**:
(3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)	**CURRENT (last year)** Cannabis Sed/hyp/anx Stim Cocaine Opioids 3 3 3 3 3 2 2 2 2 2 1 1 1 1 1 ? ? ? ? ?

[4] IF NOT ALREADY KNOWN: IN THE PAST YEAR Did your use of (DRUG) cause problems with other people, such as with family members, friends, or people at work? (Did you get into physical fights or bad arguments about your drug use?) **IF YES**: Did you keep on using (DRUG) anyway? (Over what period of time?)	**Cannabis:** **Cocaine:** **Sedatives:** **Opioids:** **Stimulants**:
(4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol (e.g., arguments with spouse about consequences of intoxication, physical fights)	**CURRENT (last year)** Cannabis / Sed/hyp/anx / Stim / Cocaine / Opioids 3 3 3 3 3 2 2 2 2 2 1 1 1 1 1 ? ? ? ? ?

CURRENT SUBSTANCE ABUSE DIAGNOSIS **(At least one item is coded "3.")?**

Cannabis	☐ Y	☐ N
Sed/hyp/anx	☐ Y	☐ N
Stim	☐ Y	☐ N
Cocaine	☐ Y	☐ N
Opioids	☐ Y	☐ N

SUPPORTING DATA: All figures and/or tables shall include legends and be clearly marked with figure/table numbers.

Data analyzed for DSMB Meeting (9/11/13)

Demographics of Randomized Participants, as of 8.31.13

Mean Age, years	52

Gender	N	Percent
Male	7	100
Female	0	0
Total	7	100

Ethnicity	N	Percent
Latino/Hispanic	4	57
Non-Latino	3	43
Total	7	100

Race	N	Percent
Asian and Pacific Islander	0	0
Black/African American	1	14.5
Mixed	1	14.5
Native American	0	0
Other	0	0
White	5	71
Total	7	100

Total Adverse Events (Percent), as of 8.31.13***

Adverse Event Organ System and Dictionary Term (MedDRA) n=7	All Adverse Events n (%)	Treatment Emergent Adverse Events n (%)
Neurologic	7 (100)	6 (86)
Numbness/Tingling	4 (57)	3 (43)
Taste Alteration	5 (71)	4 (57)
Difficulty with Concentration/Attention	6 (86)	0 (0)
Difficulty with Memory	7 (100)	0 (0)
Slow Thinking	5 (71)	0 (0)
Confusion	3 (43)	2 (29)
Language Problems	6 (86)	0 (0)
Systemic	7 (100)	5 (71)
Fatigue	7 (100)	2 (29)
Loss of Appetite	4 (57)	2 (29)
Dizziness	5 (71)	2 (29)

Itching	5 (71)	4 (57)
Sleepiness	5 (71)	1 (14)
Psychiatric	6 (86)	1 (14)
Nervousness	6 (86)	0 (0)
Depression	5 (71)	1 (14)
Suicidal Thoughts/Actions	0 (0)	0 (0)
Gastrointestinal	5 (71)	5 (71)
Diarrhea	5 (71)	5 (71)
Ophthalmologic	3 (43)	2 (29)
Abnormal Vision	3 (43)	2 (29)
Eye Pain	1 (14)	1 (14)

*****Data has been entered but not cleaned**

NOTE: Not all participants completed all 12 weeks of study at time of analysis.

Timeline Followback (TLFB) Data (Mean ± Standard Deviation) , as of 8.31.13

VARIABLE	TAP2 (n=9)
Average Drinks[$] per Drinking Day (past 90 days)	10.8 ± 7.5
Average Drinks[$] per Week (past 90 days)	62.8 ± 38.0
Average Drinking Days per Week (past 90 days)	6.1 ± 0.9
Average Heavy Drinking Days per Week (past 90 days)	4.6 ± 2.6

-Data has not finished quality check

-Heavy Drinking Day (>4 standard alcoholic drinks for men, >3 alcoholic drinks for women)

[$] standard alcoholic drink defined as containing 13.6 g of pure alcohol

Figure 1. TAP2 Drinks Per Week by Participant

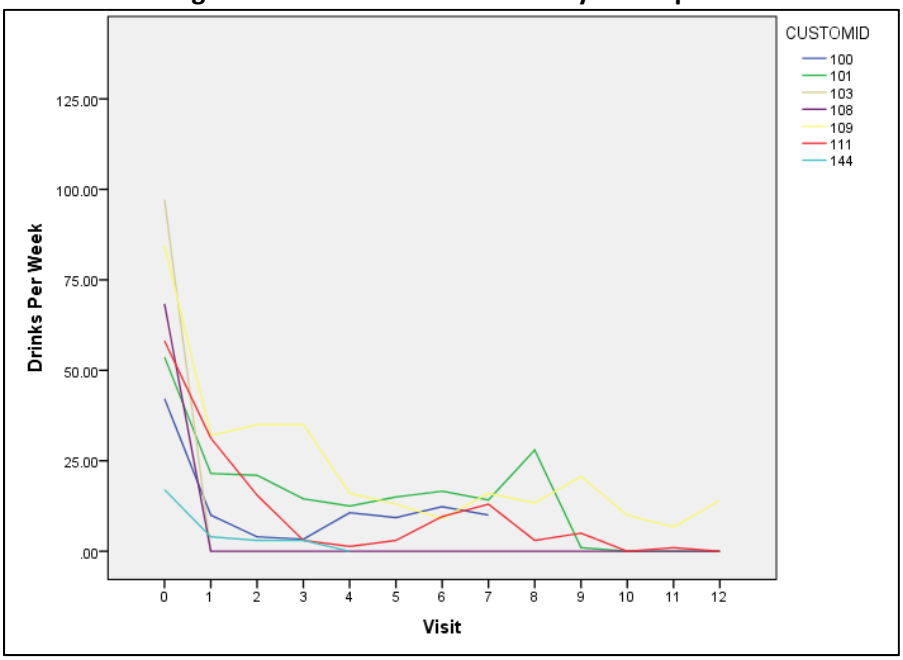


Figure 2. TAP2 Drinks Per Drinking Day by Participant

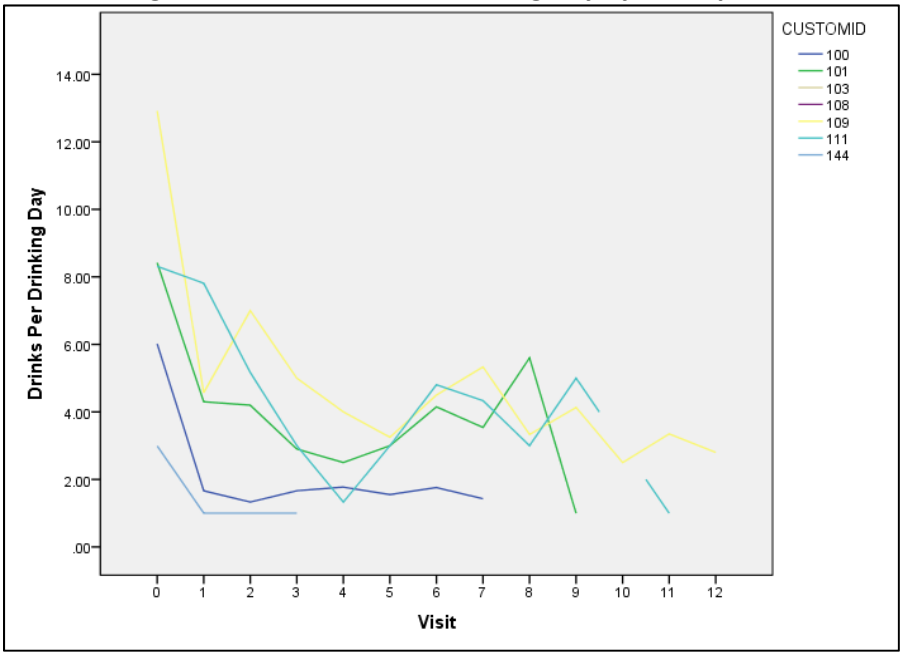


Figure 3. TAP2 Drinking Days Per Week by Participant

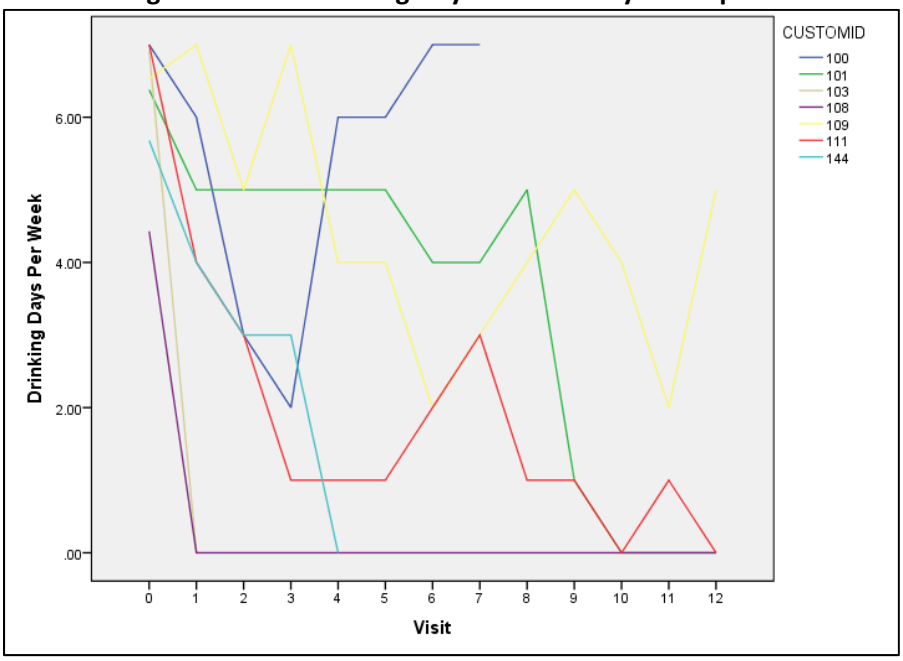


Figure 4. TAP2 Heavy Drinking Days Per Week by Participant